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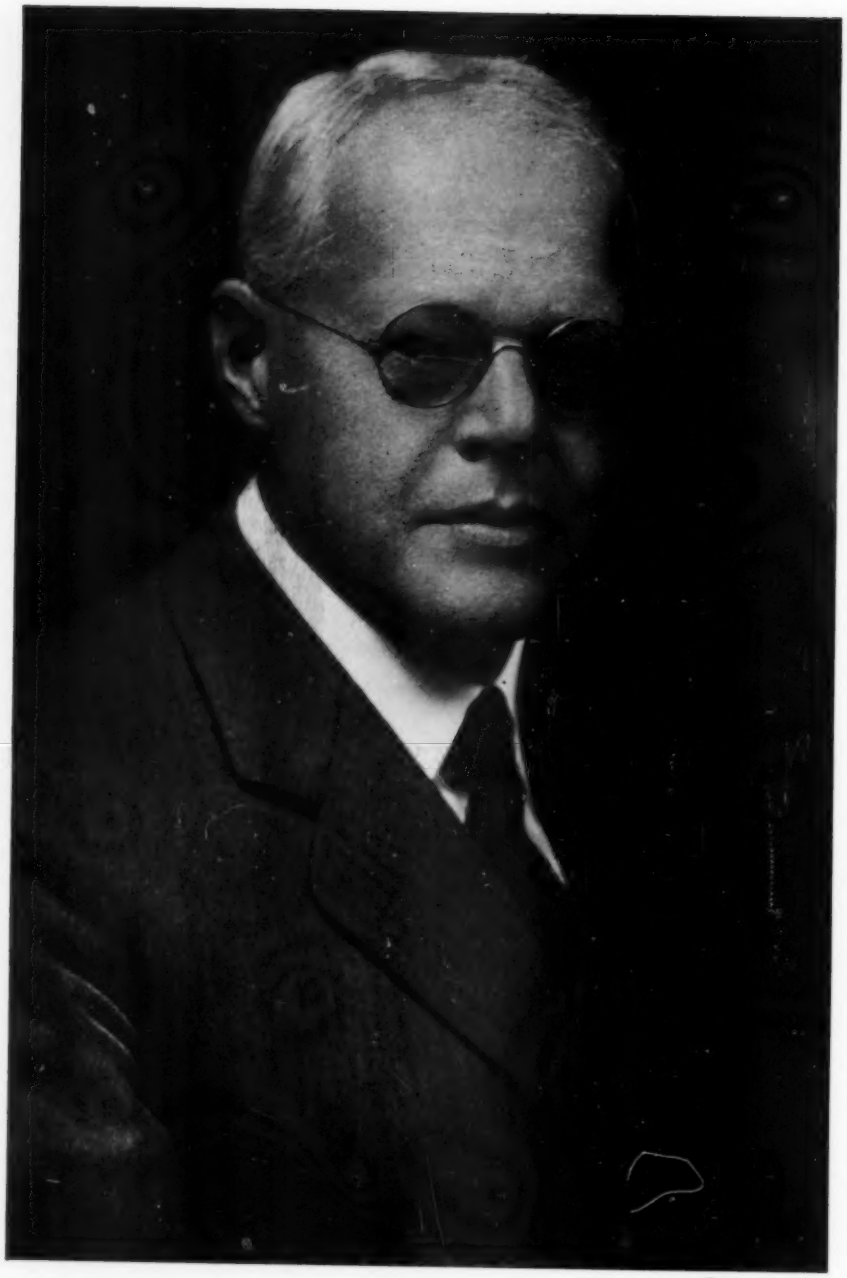
FOREWORD

To Dr. Henry K. Pancoast:

Upon the completion of twenty-five years of untiring service as Professor of Roentgenology at the University of Pennsylvania, and through the courtesy of the Editor of the Journal, this issue is dedicated to you.

Your idealism as a physician and your inspiration as a leader have stimulated all whose privilege it has been to serve under you. These manuscripts have been prepared by those who have been your associates, assistants or students.

To you, our sincere congratulations, good wishes, and the pledge of our loyal devotion!



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HENRY K. PANCOAST

UNIV. OF MICH.

HENRY KHUNRATH PANCOAST—AN APPRECIATION

IN THESE DAYS of an over-copious medical literature relating to the various fields of specialized practice—a literature to which the too hasty pen may frequently supply inconsiderate additions—a judicial estimate of a man's value to his specialty is to be formed by no superficial glance at an enumerated list of his writings in evidence of his scientific attainments, but by proper appraisal of their quality through scrutiny and analysis. Thus it may be discovered that certain fine characteristics with which some scientists may be blessed are often happily reflected in their literary communications, as evidenced by care in expression of thought, moderation in statement, consideration of alien opinion and deliberation in conclusion.

Doctor Pancoast of Philadelphia is eminently of this fortunately endowed group, but no mere literary index can alone suffice to indicate the full measure of his professional record. Care, moderation, consideration and deliberation are attributes in equal degree applicable to his manner of meeting life, to his spiritual attitude toward his fellow men. These qualities are mirrored in the allegiance of his patients, the loyalty of his medical colleagues and the pride of the University he serves so faithfully. A conspicuous pioneer of American Radiology, Doctor Pancoast has witnessed the consistent growth of his Department at the Hospital of the University of Pennsylvania over the course of twenty-five years or more, but no pen can define adequately the extent of his own contribution to its development. Even approximately to estimate this is to visualize the once daily travail of such pioneers—the quality of human patience required in the encouragement of the timorous patient, in the explanations to bystanding observers, in the labor, *solo*, (there were no "technicians") over an obstreperous Crookes tube, a flagging interrupter, a humidified static machine or a disappointing roentgenographic image rapidly evanescent amidst a dark-room atmosphere whence hope and oxygen were already departing.

The common lot of the early radiologist has been fully partaken of by Pancoast. His share of itself would have established his status as a scientific physician rather than a medical scientist, such has been his firm allegiance to Hippocratic principles as applied to the humanities, but his power of keen observation began promptly to be crystallized at the point of his pen, as is clearly revealed in the quality of even the earliest of his papers.

One of the first of these communications, prepared in the early spring of 1903 in his capacity as "Assistant Instructor in Clinical Surgery and Assistant Demonstrator in Surgery, University of Pennsylvania, and Skiagrapher to the University Hospital" and dealing with the subject of cerebral roentgen diagnosis, indicates the temperateness of his disposition and seems to portend the trend of his predilection in the roentgenologic field, for intracranial diagnosis has ever been a favorite arena for his research. Pancoast was early and thoroughly imbued with the spirit of patient exposition so essential to the progress of a method of diagnosis which, from its very nature, was at once open to suspicion and scepticism. In "The Skiagraph in Gross Brain Lesions" his attitude was conservative, and properly so, almost to the point of iconoclasm. He deplored a contemporaneous tendency to place too much confidence in the roentgenogram as to its more uncertain revelations merely because of the almost absolute proof it offers of injury to bone, of joint changes, of the presence of foreign bodies, and so on, in the extremities; but, from what he had observed by taking full advantage of the material at hand, he ventured to conclude that enough had been accomplished to prove the possibilities of the roentgen rays in this branch of Medicine to be of unlimited scope and of undoubted value.

Open expression of even such conservative opinion required more courage than may

today be realized, unless we remember the extravagant and often unjustified claims that were being made for the "x-light" in the realms of both diagnosis and therapeusis. The resulting reactionary censure would have mounted even higher had it not been for the stabilizing influence of practitioners of Pancoast's stamp, whose temperate assertions appealed to reason by virtue of the proof of *ex post facto* demonstration.

Doctor Pancoast comes justly by the qualities that are disclosed in his writings and his conduct of life. His father, Dr. Seth Pancoast (1823–1889), was descended from one of three Pancoast brothers who came to this country with William Penn; likewise a Doctor of Medicine (1852) of the University of Pennsylvania, he established a renowned practice in Philadelphia and its environs. His mother, before her marriage Miss Susan George Osborn, was also of the Society of Friends. As a young man Henry Pancoast was educated at Friends Central School in Philadelphia, from which he was graduated as First Scholar of his class in 1892. In 1898 he received his Doctorate from the Medical School of the University of Pennsylvania and at the expiration of his interneship commenced practice in Philadelphia in the autumn of 1900.

As already recorded, his early postgraduate years were in great measure devoted to the teaching of surgery, and he retained until 1904 his connection with this department of the Medical School, but his initial interest in what is now known as roentgenology must have been deep, for in 1902, when the late pioneer Charles Lester Leonard resigned his office as "Skiagrapher" to the University Hospital, young Doctor Pancoast was invited to succeed him. In addition, the University authorities, possibly influenced by the vision and pioneer research of the Philadelphia scientists White, Goodspeed, Leonard, Davis and Willard, in wisdom foresaw the ultimate position of the "new science" in the Medical School curriculum and created for Pancoast the teaching position of "Lecturer on Skiagraphy" in 1905. As such, with unceasing labor and unselfish devotion to his work, he guided the ever-expanding functions of practice and of teaching through the year 1911, and in 1912, by a corporate act clearly indicative of a thorough appreciation of his sterling worth, Pancoast was elevated, without the usual processes of intermediate increase of rank, to the Chair of Roentgenology at Pennsylvania, one of the earliest of the medical schools to create so exalted a teaching position in this young branch of science.

No new Professorship could have been established under more favorable auspices, nor could any man have dignified it more completely. Under his gentle but firm direction the Department of Roentgenology at the University of Pennsylvania has steadily developed, in both School and Hospital, its salutary dual function of teaching and healing for five and thirty years.

Of Pancoast's works—and by this term is meant the constructive influences of his precept and example on the evolution of roentgenology, whether in the laboratory in front of screen or illuminator or on the teaching platform—what are the ones that appear to stand preëminent among others? In view of a record so replete with accomplishment, this question were hard to answer, perhaps, but on this point it would seem that contemporaneous opinion, however humble, might prove the most accurate. Only from intimate knowledge of radiological expansion through contact with it from year to year can the story of its growing demands, and the outcome of the human effort to meet them, be accurately recited for the modern student of scientific history. What seems to be the mere molehill of today may well have been the mountain of yesterday, so does the passage of time alter the proportion of things as viewed through the lenses of scientific advancement; in proof of this, the records show that it was the persistent research of Pancoast as a roentgenologist that helped to reduce what was a very real mountain in the path of the early roentgenological diagnostician of alimentary disorder.

This apparent barrier to progress was the frequently encountered toxicity of a most useful radiopaque salt—the subnitrate of bismuth. Harmless in ordinary doses and even a valuable therapeutic agent, in quantities essential to alimentary roentgen diagnosis, it was found often to produce subjective symptoms of an alarming nature. Pancoast and his co-investigators found this toxicity to be due, not ordinarily to the impurity of arsenical adulteration, as had been generally supposed, but in fact to the post-ingestive release of deleterious nitrites by the conversive action of the gastric HCl on the subnitrate salt. The result of this inquiry was a general substitution of the subcarbonate of bismuth and occasionally the oxychloride, both inert in the presence of the gastric secretions, for roentgenographic purposes. These experiments paved the way for the ultimate adoption of the salts of barium that are now generally employed for this purpose. In consequence, there developed in 1906 a most appreciative attitude on the part of American roentgenologists toward this specific investigation wherein Pancoast, proceeding from their standpoint and sharing their common perplexity, had cooperated to discover the cause and the means of its removal.

It was several years later that Doctor Pancoast pursued another inquiry of kindred nature—a roentgen study of the possible effect of moderate doses of some of the opium derivatives on the human alimentary tract. The outcome of this research had likewise a most practical application, in view of the fact that early attempts at fluoroscopic study especially, were so frequently impeded by the physiologic action on alimentation of opiates, and also of carminatives and cathartics, administered clinically without consideration of the requirements of proper fluoroscopy. This valuable pioneer work contributed materially to the establishment of a more definitive coordination of the functions of clinician and roentgenologist.

From the day, in 1903, of his most careful report to the fourth meeting of the American Roentgen Ray Society of his results of roentgen treatment in nearly one hundred cases, the practice of roentgen therapy has held an attraction for Henry Pancoast. With the reading of that paper he appeared on the field of action just in time to encounter the already waning effects of the pure empiricism of primitive effort in treatment by irradiation. It remained for him and those of the strong Philadelphia group of which he was one, to develop the first early attempts at dosage control, especially in connection with deeply seated disease, that were being made in America during the year 1903.

Without question, Pancoast must have been prompt to scan and analyze the astounding report of Nicholas Senn, submitted the same year, of a case of splenomedullary leukemia treated, in the hands of Pusey, by roentgen irradiation of the spleen. Moreover, he was in close clinical association with certain Philadelphia internists of high standing who had become deeply interested in this subject upon the appearance of Senn's report. This contact afforded Pancoast ample material for observation and study. Taking advantage of this opportunity, he published from 1906 to 1922 at least ten authoritative papers on the clinical results of roentgen irradiation in disorders of the blood and the blood-forming organs. This investigation and the impulsion it gave to conservative radiation therapy may properly be classed as one of his prime achievements.

From the earliest days of his attraction to the "new science," Doctor Pancoast's loyalty to the welfare of the scientific societies formed from time to time for its study and practice has been second only to his devotion to his daily work. Becoming a member of the American Roentgen Ray Society in 1903, he was closely identified with the local arrangements for its successful fourth annual meeting, held that year in Philadelphia under the Presidency of Professor Goodspeed of the University of Pennsylvania, who, by the way, is the only physicist to have held this office. Two years later, Pancoast was one of a group called together by the late Charles Lester Leonard to form the Phila-

delphia Roentgen Ray Society, which has consistently grown to its present vigor and usefulness. Since the year 1903 Henry Pancoast has maintained his effective service in the interests of the American Roentgen Ray Society; this was by no means relinquished, as sometimes happens, with his election to its Presidency in 1913, following a most active official year as Secretary.

He has been an almost yearly contributor to its scientific programs, on both diagnostic and therapeutic subjects. His first communication was presented in the year of his election to membership, as above mentioned. It was fortunate that this paper happened to deal with the general therapeutic effect of roentgen rays, for it came at a time when this mode of treatment was distinctly on trial before a medical world prone to contemptuous scepticism. Bulwarked by a mass of illustrative material, the report was of the utmost importance, and by no one could this subject have been dealt with in more complete rationality. It at once established Pancoast's position in the estimation of those who cherished the future of radiology as a factor in the practice of scientific medicine. That position he has occupied without hair-breadth deviation over the course of his professional life.

In the field of radium therapy, the record of Henry Pancoast holds equal prominence as an exemplar of the highest ideals of its practice. In the early years of its existence, his colleagues of the American Radium Society were prompt to recognize this fact; accordingly it was through a natural evolution of the beneficial activities of that organization that he became its Secretary in 1917 and its President two years later. By a similarly due and natural process he was elected to Fellowship in the American College of Radiology, of which he became a Chancellor the year following the date of its foundation. He continued to occupy a seat on the Board of Chancellors for four years and was made the President of the College for the year 1933–1934. Two years previously, he had been elected to the Chairmanship of the Section on Radiology for the scientific assembly of the American Medical Association, which convened in New Orleans in 1932. Doctor Pancoast is also a member of the Radiological Society of North America.

With this splendid record of allegiance to the high aims of his specialty through loyal association with groups of its most eminent practitioners, it is hardly a matter of surprise that Henry Pancoast was chosen to be the President of the First American Congress of Radiology, which met at Chicago in the autumn of 1933.

To be thoroughly sensible of the versatility of Doctor Pancoast's instinct for investigation, we must examine the history of his earlier work of the year 1916. It was then that he and Dr. H. R. M. Landis of the Henry Phipps Institute became interested in the increasingly important subject of pneumonoconiosis through Landis's suggestion that a roentgenologic investigation be made of the respiratory apparatus of workers in the various "dusty" occupations. Research was consequently undertaken by them in association with Dr. T. G. Miller, the report of which closely followed that of Lanza and Childs of 1917. A continuation of this absorbing study has occupied Pancoast and other coworkers at intervals for over fifteen years, with the result that in many papers he has described in detail the roentgen evidence furnished by these thoracic conditions, establishing the fact that the organic dusts do not produce lung changes. Beside his contributions to the periodic medical and industrial literature, a monograph on this subject appeared in 1926 from the combined pens of Dr. Pancoast and Dr. E. P. Pendergrass. In connection with his earlier effort in this field of the dust diseases, Pancoast was from 1923 to 1928 appointed Consulting *Physiologist* to the United States Bureau of Mines, a title which causes a whimsical smile to accompany his retrospective allusion to it.

The opportunity for War service appealed to Henry Pancoast's patriotic spirit. His duties in connection with the Medical Corps of the Navy were discharged with the

fidelity that has characterized all his acts. He was commissioned in 1918, with the grade of Assistant Surgeon, rank of Lieutenant (junior grade) and in 1919 was retired to the Inactive List with the grade of Passed Assistant Surgeon, rank of Lieutenant.

The corporate act of wisdom that raised Doctor Pancoast to the Presidential Chair of the First American Congress of Radiology in 1933 was the culminating event of one of his most productive years—a year that gave him opportunity to contemplate, from the high and broad plateau upon which his life's fruitful journey has placed him, "the widening field of radiology"* and also to visualize, in his address to the Congress, "the future of radiology as a medical specialty."† Acting on the beneficent impulse of the true physician he offered, in this address, a diagnosis of the causes of certain untoward tendencies which react in a manner detrimental to the best interests and the best services of radiology, as well as the following remedial measures to counteract them: the proper education and training of radiologists; the teaching of the medical student or interne so that he may be able to decide between useful and useless radiological assistance in his future problems; the recognition of radiology as strictly medical practice to the exclusion of the commerical laboratory; a cultivation of the moral effect of radiological societies; the creation of a Qualification Board for the approval of radiologists.

In the comparatively few years that have ensued since these recommendations were made, the influence of Pancoast and others of his caliber and trend of thought has brought about a realization of nearly all five of them. In the ultimate establishment of the American Board of Radiology and in its present functional efficiency, he can pridefully see the fructification of the last and most important.

On the same occasion, in his evaluation of the present and future status of his specialty, Pancoast's breadth of mind and generous nature are manifested in the following doctrine:

" . . . we, as radiologists, are apt to think that radiology is entirely what we have made it by our own collective exertions and experiences. In this view we are mistaken and, were it true, we would not have advanced to the position we now occupy. . . . We must not lose sight of the fact that our progress has been materially abetted by a considerable amount of assistance from outside sources. The physicist Röntgen helped us on our way, and others of the world's most renowned men of the same scientific group have helped . . . in our advancement."

To illustrate this truism specifically, he further refers to the physiologists, chemists, dermatologists, surgeons and internists who have done so much as allies of Radiology to promote her progress. What spirit more worthy of inculcation on the minds of those who, in maintaining that the eminence she occupies today has been totally self-attained, have evidently forgotten her history?

Thus it requires but a simple chronicle of this man's career to create an appreciation of its utterly constructive influence on his own specialty and on medicine in general. It is through such appreciation that those of us who have especial reason to admire his qualities are gratified by the opportunity to voice it on this twenty-fifth anniversary of the inception of his Professorship at the University of Pennsylvania. It is peculiarly satisfying to the older of us who are marching onward with him. Advancing by his side, his presence recalls to memory the fading aura of a departed day—that happy day when, within a great city that once had been the colonial village home of "Poor Richard," versatile and wise, a small group of earnest pioneers whose hearts with ardor were electrified as by the tiny spark from Franklin's key or the static field of Röntgen's tube, had forgathered for mutual instruction and enlightenment. Christened in honor of the great physicist of Würzburg, this young Philadelphia society remained, unhappily, not

* The widening fie'd of radiology. *Pennsylvania M. J.*, 1933, *37*, 206.

† The future of radiology as a medical specialty. Am. J. Roentgenol. & Rad. Therapy, 1933, *30*, 711.

long intact, for the martyred Kassabian and Leonard soon departed in their glory, leaving the rest of that little group to continue the work they had found so fascinating and for which they and others like them had given life itself. On such men as Henry Pancoast, faithful and steadfast, they pinned their high hopes for the future of radiology. Wholly inadequate would be any attempt to show how thoroughly he has justified their confidence!

PERCY BROWN

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THE HEALTHY CHEST*

By EUGENE P. PENDERGRASS, M.D., *and* PHILIP J. HODES, M.D.
PHILADELPHIA, PENNSYLVANIA

FAMILIARITY with the roentgen appearances of the healthy chest is a prerequisite for anyone who attempts to properly interpret chest roentgenograms. Unfamiliarity with normal variants and with the modifying influences of a faulty technique not infrequently results in misinterpretation, with an attendant chain of difficulties. A common example of such an error is the diagnosis of pulmonary tuberculosis, pneumoconiosis and silicosis based on the presence of prominent truncal shadows. The clinician, in arriving at an ultimate conclusion in chest conditions, places so much reliance on roentgen interpretation that another discussion of the healthy chest seems justifiable, in spite of the excellent material already available on the subject. Furthermore, over ten years have elapsed since the publication of the reports on the chest by the National Tuberculosis Association Committee,[31,32] and of other less well-known articles on the same subject. Within more recent years, improvements in certain technical factors and apparatus have created marked variations and changes in the roentgenographic appearances of some of the chest structures. In view of such facts, therefore, a review, and where necessary a revision, of the more pertinent aspects of the chest problem, both in health and in disease, seems necessary.

The various tissues demonstrable in the chest roentgenogram will be discussed individually and in the order in which they are taken up in our routine consideration of such an examination. To follow a definite system in the study of any roentgenograms prevents the overlooking of, in some instances, obvious conditions.

THE SOFT PARTS

The approximate development of fat and musculature can readily be determined from the roentgenogram. The density of the axillary fold frequently serves as an index of the patient's state of nutrition. A loss, as well as a gain, in weight can easily be determined by comparison of the thickness of the soft parts in those instances in which repeated chest exposures have been made. Sometimes, apparent roentgen evidence of diffuse pulmonary haziness and lung pathology may be explained by unusually thick soft parts. Examples of such instances include the well-developed pectoral folds in men, large breast shadows in women, and the appearance of the female chest when one breast has been removed.

The nipples of the breasts and pigmented moles may produce shadows in the roent-

* From the Department of Radiology, Hospital of the University of Pennsylvania, Philadelphia, Pa.

genogram that simulate those of metastatic nodules or other pathological processes. Shadows of air and fluid levels, due to abscesses within soft parts, may cause uncertainty and have been misinterpreted as lung abscesses. In roentgenograms of infants, a few days to a few weeks of age, redundant folds of some of the tissues covering the thoracic cage will produce shadows that are similar to those of a pneumothorax. Careful study of these shadows, however, should aid in determining their identity. In the examination of infants, a restraining band is usually used to fix the chest during the roentgen exposures. Such fixation may produce longitudinal folds of the soft tissues at the junction of the lateral chest wall with either the anterior or posterior walls. In the roentgenogram, the shadow of these folds is superimposed upon the peripheral shadows of the thoracic cage and lung fields, and thereby, in position, simulates a pneumothorax. If the shadows are carefully analyzed (the hill of tissue appearing dense and the valley, less dense), it is possible, in almost every instance, to properly identify their nature. The confusion caused by this shadow density can be compared to that caused by the ear in an examination of the infant mastoid.

Other soft tissue shadows, such as calcifications of vessels, angiomas, tumors, thyroid, and lymph nodes, may be observed in the neck and axillae. Shadows of soft tissue masses (benign or malignant) and enlarged lymph nodes can be demonstrated in the axillae, neck or supraclavicular fossae. Interstitial emphysema is easily recognized. Abscesses and cellulitis will cause changes in the shadows of the normal tissues and obscure the tissue planes.

THE BONES

The bony thorax can be fairly well visualized in the chest roentgenogram in the anteroposterior, posteroanterior and lateral projections.

In the *posteroanterior* and *anteroposterior views*, with the sternal ends of the clavicles equidistant from the spine, in order that the chest be symmetrically placed, one can see the clavicles, the upper end of the humeri and the scapulae, the ribs, the cartilages when ossified, and the alignment of the thoracic spine. In a few instances, one can see the irregular appearance of the rhomboid fossae on the under surface of the inner fifth of the clavicle. This may be unilateral or bilateral and should not be mistaken for a bone lesion. Occasionally, one can see the shadow of the foramen of the supraclavicular nerve, near the upper aspect of the middle of the clavicle.[39] The epiphyseal development of the inner end of the clavicles can be readily demonstrated, as can epiphyseal centers in the humeri and scapulae. The normal variants of the ribs, such as bicipital and cervical rib, should be noted. A mental note should be made as to the density of the ossification of the bones. Not infrequently, decreased bone density, caused by some condition such as parathyroid disease, or even localized areas of bone destruction from metastatic malignancy, will assist in directing the attention of the clinician to the primary cause of the patient's complaint. Recognition of erosion of the under surface of the ribs may lead to a diagnosis of coarctation of the aorta. Ossification of the costal cartilages is of very little significance. We place no reliance on the old dictum that ossification is evidence of a chronic bronchitis. In general, ossification increases with age, but occasionally it is found well advanced in thin young women. In such instances, it may be difficult, at times, to interpret structures near the midline, due to the superimposed shadows of the costal cartilages. Oblique views are of great assistance in these patients. There seems to be very little difference in the width of the intercostal spaces in the absence of pleural involvement. In older individuals with increased aeration or emphysema, the intercostal spaces may be slightly wider, but the important manifestation is that the ribs

assume a more right-angled position with the spine. The alignment of the thoracic spine can be readily demonstrated. Minor degrees of scoliosis do not interfere with study of the chest, but marked scoliotic changes, on the other hand, tend to obscure the shadows of the structures in both lung fields, due to the shadows of the spine on one side and the closeness of the ribs on the other.

In the *lateral view*, one can see the ribs, portions of the shoulder girdle and the thoracic spine. The spine is readily visualized, but superimposed shadows of lung structures are confusing in evaluating bone detail. In infants, the notched appearance of the anterior aspect of the vertebral body, resulting from incomplete ossification of the primary and secondary centers, and the point of entrance of the blood vessels are well shown. In adolescents, shadows of the secondary centers of the cortical plates on the upper and lower aspects of the vertebral bodies are seen. In adults, the body of the vertebrae may, or may not, show hypertrophic changes, and even calcification of the nucleus pulposus.

Usually there is a gentle, double curve to the spine, concave posteriorly above and slightly convex, or straight, below. In kyphotic individuals, the anteroposterior diameter of the chest may be greater than the transverse. The vertical diameter of the body of the vertebrae and the intervertebral discs increases slightly from above downward.

THE PLEURA

The parietal pleura is so thin that it does not cast a shadow which can be seen in the roentgenogram unless it is thickened and diseased or obliterates some portion of the costophrenic sulci. Very slight thickenings of the parietal pleura may be suspected in those instances when there is interference with the costal expansion, especially when the process is unilateral.

In anteroposterior roentgenograms of the chest made with the Potter-Bucky diaphragm, the reflection of the pleura, ligaments and muscles over the vertebral column produces a straight line shadow on each side of the spine. Disturbance in this normal straight line may occur in spinal caries, bone tumors, some spinal cord tumors that emerge from the spinal canal, and pleural collections occurring in the vicinity of the vertebrae.

In this country particularly, where one finds many references to the apical cap (thickening of the visceral pleura over the apices of the upper lobes), it is a wise roentgenologist who recalls that there are other structures whose shadows create a similar appearance in a similar position. Subcostal muscles, in the oblique views, may be misinterpreted as thickened pleura.

The roentgen appearances of these various anatomical structures have been reemphasized by Knutsson,[13] whose observations are briefly abstracted. On the posterior portion of the thoracic wall, the internal surfaces of the ribs are covered with subcostal muscles. In the lateral aspect of the thorax, the muscle lining disappears. The narrow muscle layer on the inner aspect of the ribs produces a shadow, seen only in the oblique view, with one exception, which gets thinner from above downward and disappears entirely in the region of the costophrenic sulci. In pleurisy, on the other hand, the pleural thickening usually gets thicker from above downward (Fig. 1), and may obliterate the sulcus. The thickness of the muscle shadow depends upon the muscular development of the individual. In the upper thorax, the muscles extend laterally, far enough to be seen in the posteroanterior and the anteroposterior projections. This structure is called the "companion shadow of the second rib." Mesial to the angle of the second rib, there are no subcostal muscles, and the shadow here is produced by the connective tissue. The first rib, likewise, has a companion shadow which is produced by a sheet of connective tissue interposed between the posterior part of the dome of the pleura and the first and, to a certain degree, the second rib. The fol-

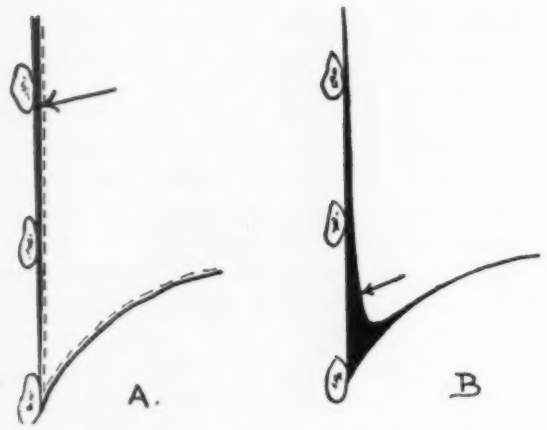

Fig. 1. *A.* Schematic presentation of intercostal muscles demonstrating the decrease in the thickness of the muscles as they approach the diaphragm.

B. Schematic presentation of pleural thickening which becomes more prominent near the diaphragm. (Knutsson.[13])

lowing structures are situated in this interspace: the last cervical ganglion of the sympathetic, the supreme thoracic artery and vein, and the first thoracic nerve. The "companion shadows of the first and second ribs," as well as those produced by the subcostal muscles in the oblique views, are symmetrical on the two sides. This fact should be of assistance in differentiating these shadows from those created by pleural thickening. The pleura does not calcify under normal circumstances.

The visceral pleura covers the different lobes of the lungs and ordinarily does not cast a shadow that can be seen in the roentgenogram, except in the instance of the azygos and other accessory lobes (Fig. 2). At times, straight and very thin shadows of the interlobar lines can be seen in the chests of healthy individuals. We have felt that such pleural shadows represent a permanent thickening of the pleura from a pre-existing infection. Furthermore, such slight thickening of the interlobar pleura is capable of producing shadows because the roentgen rays are projected in their axial plane (Fig. 3). This conclusion is supported by the frequency with which a shadow of the interlobar pleura is found in one roentgenogram of a stereoscopic pair and not in the other. Any interlobar thickening not observed in an axial plane will, nevertheless, produce shadows in the roentgenogram, which, when superimposed upon those of the lung fields, will create an increased density. If such a density is not recognized in its true relation, it may be mistaken for an intrapulmonary lesion. In disease, the visceral pleura rarely, if ever, becomes as thick as the parietal pleura. Clark[3] believes that, when adhesions have formed, the increase in the thickening of the pleura in the lower chest and around the heart, as compared to that occurring in the upper chest, is due in part to the relatively more powerful movements of structures such as the domes of the diaphragm, the flaring of the ribs, and the pulsation of the heart.

The position of the interlobar fissures, as we usually see them, are referred to by

Fig. 2. Azygos lobe. *a*, azygos lobe; *b*, azygos vein; *c*, upper lobe; *d*, superior vena cava; *e*, pulmonary artery.

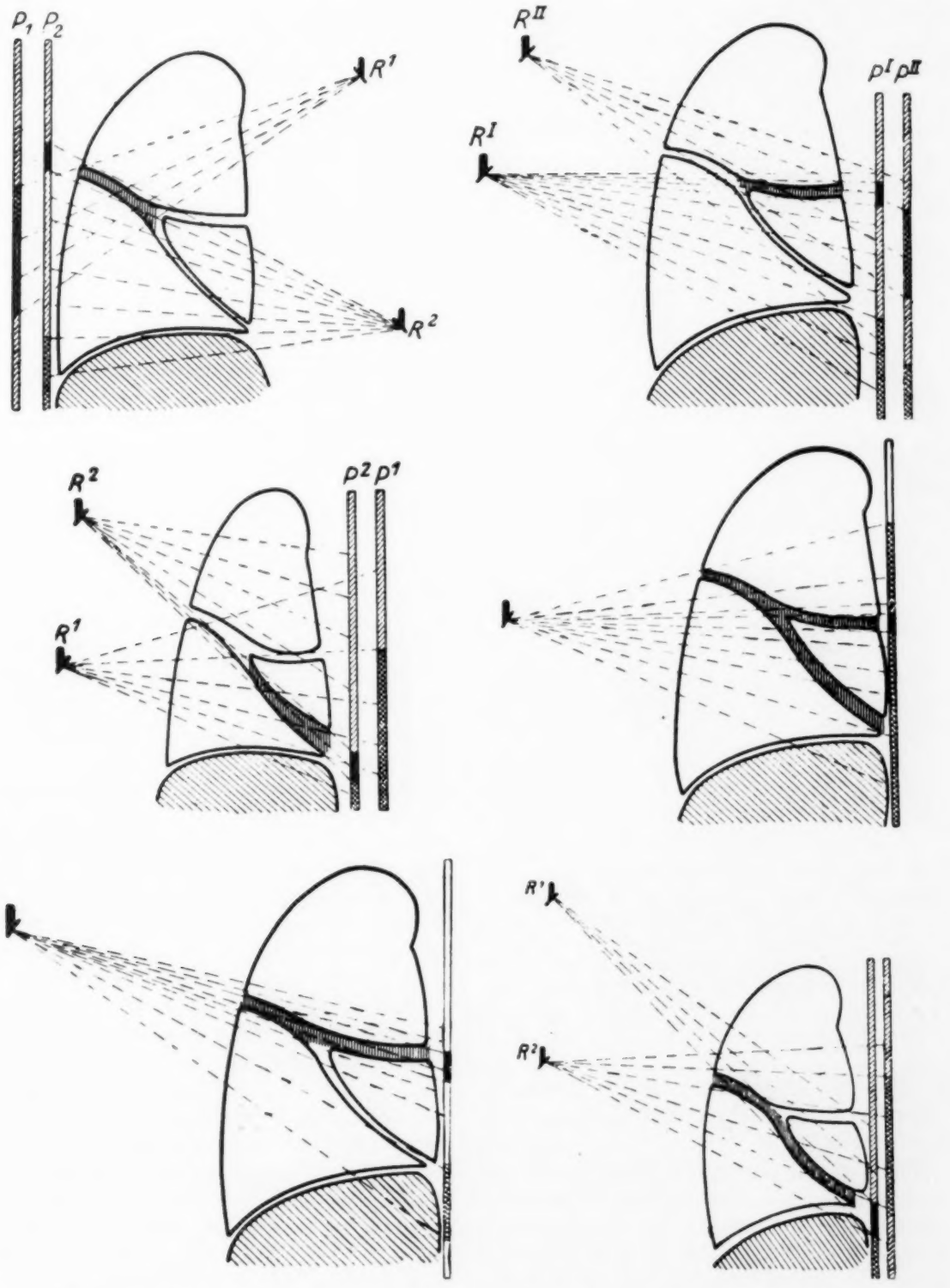

Fig. 3. Diagrams showing how the direction of the central ray influences the roentgen manifestations of interlobar disease. The central ray must be projected along the axis of the interlobar pleura for optimum contrast. (Liebmann.[15])

Liebmann[15] (Fig. 4). The technique for demonstrating lesions of the various interlobar regions, in addition to the conventional anteroposterior, posteroanterior, oblique and lateral views, includes those in

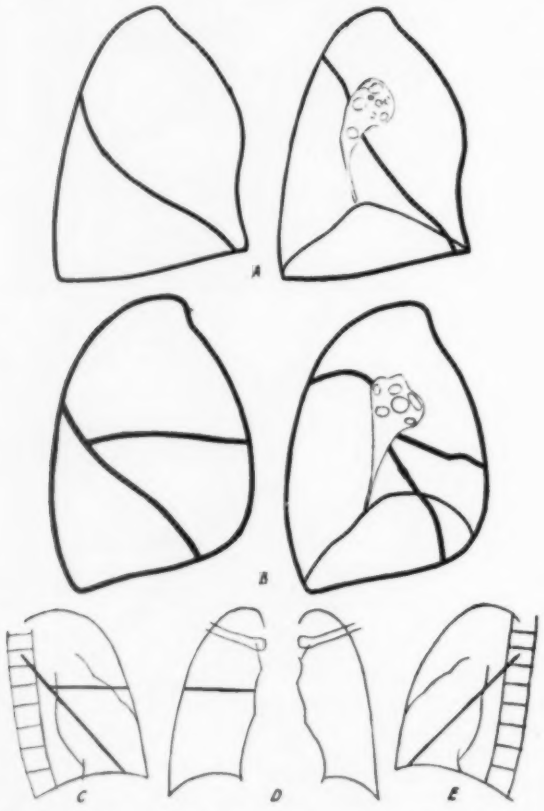

Fig. 4. *A*, position of interlobar fissure in the right lung; *B*, interlobar fissures in the left lung; *C*, relative positions of the fissures with the patient in the left lateral position; *D*, position of the right interlobar fissure with the patient in the anteroposterior position; *E*, position of the interlobar fissure with the patient in the right lateral position. (Liebmann.[15])

which an effort is made to project the roentgen rays in the axial plane of the interlobar fissure (Fig. 3).

The visceral pleura is reflected over the mediastinal structures and does not cast a recognizable shadow. In disease, however, it may produce changes which can be observed in the roentgenogram. In certain instances, when the mediastinal pleura is symmetrically involved, relatively marked changes may be passed over as of no significance, because of the similarity of the shadow complex to that of the normal. Liebmann[15] illustrates the changes of the visceral pleura as shown in Figure 5.

In infants, folds of skin may produce shadows that are similar to those produced by a small pneumothorax. Anomalous lobation of the right lobe of the liver may create a shadow in the lateral view that simulates that of an interlobar collection.[14]

THE MEDIASTINUM

In roentgenograms of the chest, we prefer an exposure that will show the shadow of the trachea down to, and including, its bifurcation. In the posteroanterior or anteroposterior roentgenograms, with the patient placed correctly, the shadow of the trachea in the neck will be seen in the midline. Deviation to the right or left of the midline above the level of the clavicles may result from rotation of the head, and must be differentiated from displacements of other origin. Below the clavicles, the trachea continues in its midline position until it reaches the level of the aorta, where it deviates slightly to the right in roentgenograms exposed during the inspiratory phase of respiration. In adults, in roentgenograms made in the expiratory phase, the trachea is displaced slightly to the right throughout its thoracic position; and in infants, there is often a marked buckling of the trachea to the right during expiration. In all instances, the shadow of the lumen of the trachea is fairly uniform, although its lumen decreases slightly from above downward. Just above the trachea, the laryngeal portion of the upper respiratory pathway is narrowed and produces a funnel-shaped shadow, with the apex of the funnel cephally placed. In children, the tracheal lumen may decrease as much as 50 per cent during expiration, although this observation may not be very apparent in the roentgenogram.

The tracheal cartilages, especially when ossified, aid greatly in the demarcation of the trachea.[29] Careful inspection of the

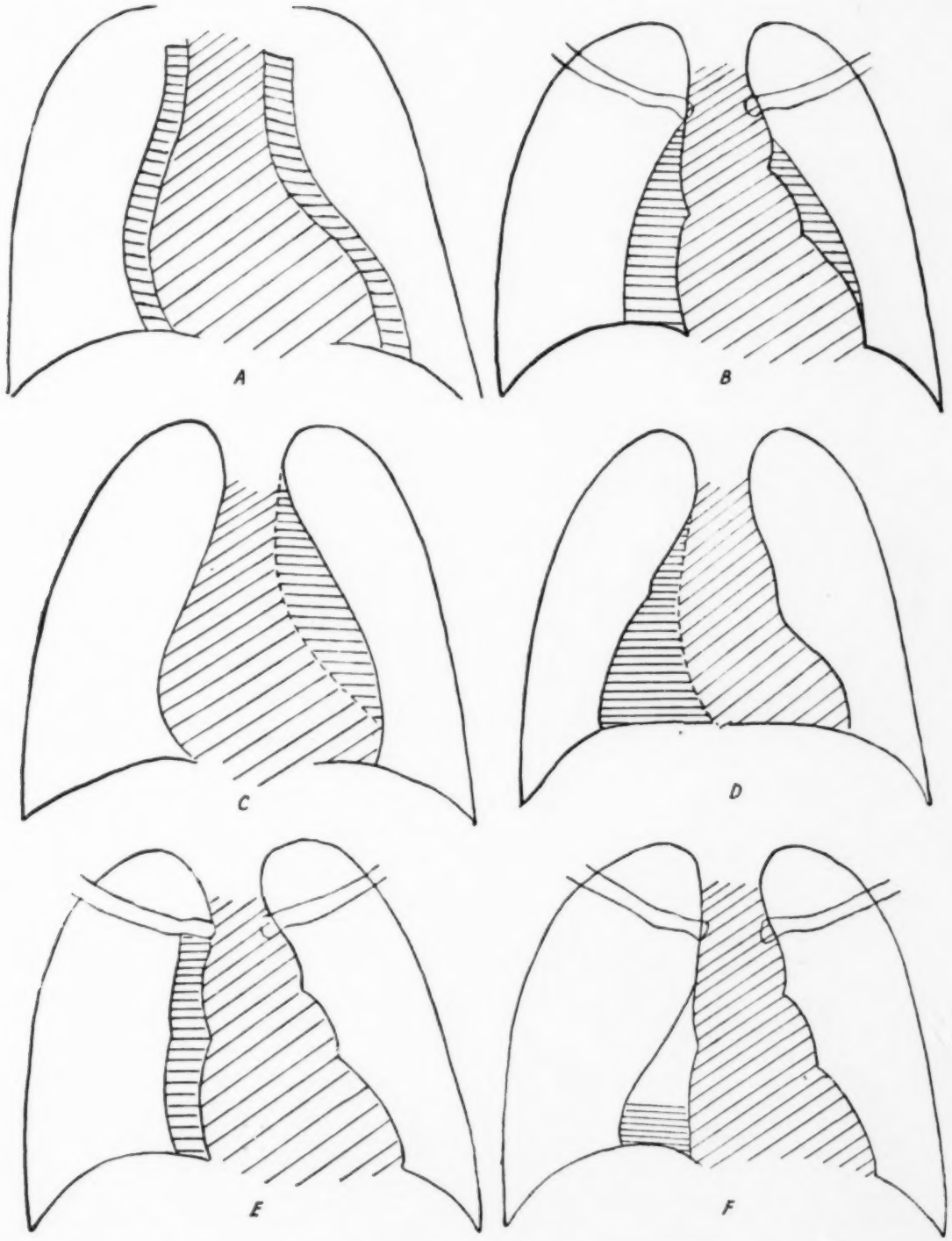

Fig. 5. Diagrammatic presentation of changes in the visceral pleura. *A*, beginning bilateral mediastinal pleuritis, enlarging the cardiac silhouette; *B*, bilateral anterior mediastinal pleuritis, simulating cardiac enlargement; *C*, left-sided mediastinal pleuritis; *D*, right-sided mediastinal pleuritis, enlarging the cardiac silhouette, suggesting pericarditis; *E*, posterior right-sided mediastinal pleuritis with a ribbon-like paravertebral shadow; *F*, anterior right-sided mediastinal pyopneumothorax. (Liebmann.[15])

shadow of its contour will not infrequently show evidences of compression or deviation that may prove significant. As a rule, the lumen of the trachea is larger in men than in women. Its caliber is not uniform throughout, becoming progressively narrower as it approaches the bifurcation.

The level of the bifurcation of the trachea varies with age. In the new-born child, it lies at the level of the third, although it may be as low as the fourth, thoracic vertebra.[29] In adults, it usually divides at the level of the intervertebral disc between the fourth and fifth, or as low as that between the fifth and sixth, vertebral bodies. It is well to remember, however, that the relationship in the cadaver may vary considerably from that in the living. Likewise, the level of the roentgen tube may cause discrepancies in the level of the bifurcation and the carina.

The angles made by the bifurcating bronchi with the trachea vary with age and from one another. In children, the right bronchus may form an angle with the trachea varying from 10 to 35 degrees while the left bronchus forms one of 30 to 50 degrees.[29] In adults, the angle of the right bronchus is approximately 20 degrees and the left, 40 degrees. The eparterial bronchus sometimes branches directly from the trachea.

The shadows of the trachea and the right and left bronchus can readily be seen in the oblique and lateral projections of the chest. In the lateral view, the trachea may be followed from the suprasternal region down to its bifurcation. During inspiration, the entire trachea moves downward and slightly forward, unless fixed by mediastinitis. In children, the trachea buckles during expiration. This posterior buckling and diminished lumen of the trachea during expiration is frequently misinterpreted as changes due to thymic enlargement. Such an appearance during inspiration is significant and may represent thymic enlargement or a congenital heart. Encroachment upon the lumen of the trachea is usually on its posterior aspect, or membranous portion, even though the cause of the encroachment may be situated anterior to the trachea. The esophagus is situated behind the trachea.

The soft tissues flanking and surrounding the trachea have been discussed by Dann.[4] His investigations have helped substantially in identifying the structures producing these shadows. The right border of the supracardiac portion of the mediastinum is formed by the superior vena cava and innominate artery, while the most lateral margin of the mediastinal shadow is almost invariably formed by the superior vena cava (Fig. 6). The more medial density is a combination of the vena cava and the ascending aorta, which lies slightly anteriorly and to the left.[2] The space between the vena cava and aorta, as described by Dann[4] in his studies in young cadavers, is rarely seen roentgenographically. However, a markedly distended aorta may approach the right border of the superior vena cava and, in some instances, actually forms the right border of the superior mediastinum. When enlarged shadows of this general configuration are seen, one should consider a substernal tumor, aneurysm of the innominate artery, and diverticulum of the esophagus. Roentgenoscopic observations of the changes in the shadows during the grunt of forced expiration and a study of the esophagus may assist in differentiating between substernal thyroids, innominate aneurysms and esophageal diverticula.

The left border of the supra-aortic portion of the superior mediastinum is formed by the soft tissue shadows of the left common carotid and subclavian arteries. The recurrent laryngeal nerve lies to the left of the trachea. The shadow of the aortic arch is usually seen extending beyond the left border of the spine. With increasing age, its knob-like contour becomes more prominent, until it is most pronounced during the arteriosclerotic period of life. The left posteroanterior oblique view of the chest permits excellent visualization of the aorta and, when used in conjunction with roent-

genoscopy, gives valuable information concerning aortic dimensions and elasticity. The aorta follows a more sagittal course in narrow-chested individuals than in flat-chested persons. Increases in prominence in the outline of the shadow of the aortic knob may result from syphilis or hypertension, while an absence or decrease in the outline of the knob suggests either coarctation or right aortic arch.

estimations, the roentgenologist must concern himself with the pulsations and the mobility of the heart and any abnormal densities. There are many conditions, such as congenital deformities of the chest and acquired affections, such as pneumothorax and hydrothorax, which may exert profound influences upon the heart. Examinations must be made in the anteroposterior, posteroanterior, oblique, and lateral views,

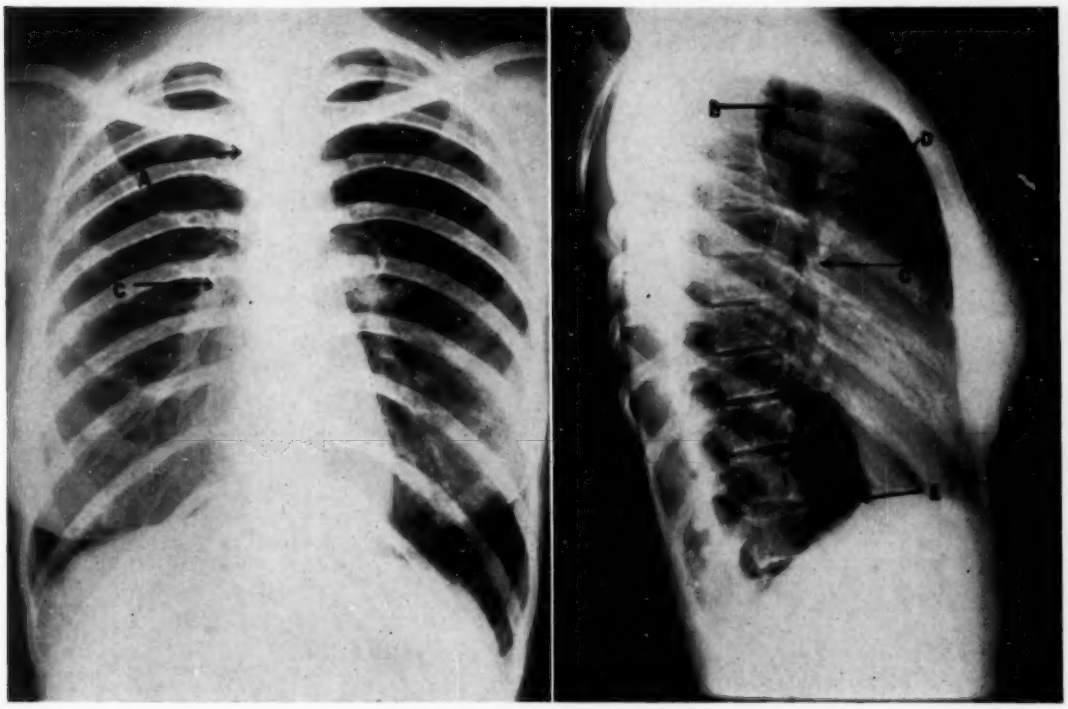

Fig. 6. Healthy adult chest. *A*, superior vena cava; *B*, trachea; *C*, hilum or root zone; *D*, pre-aortic space; *E*, a composite shadow, made up of the inferior vena cava, the phrenopericardial ligaments, and possibly also fluid in the cul-de-sac.

The pulmonary artery is seen best with the patient in the anteroposterior or right antero-oblique positions. It lies just to the left of the base of the aorta, nestled within the confines of the aortic arch. Sometimes it is seen better after a cough, which serves to separate it from the aorta.[30]

In recent communications, O'Kane, Andrew and Warren[30] and Margolies[19] reëmphasize the importance of the roentgenographic and the roentgenoscopic examinations in determining the size and shape of the heart. In addition to these

in order to assure adequate study of the heart. The most important view is the left antero-oblique view, but the degree of rotation and the optimum position for a roentgenographic demonstration must always be guided by the preceding roentgenoscopic impressions.

Under normal conditions, the heart in thin individuals lies in the vertical position, whereas in the more stocky, broad-chested person, it assumes a more transverse position. Furthermore, patients with round chests more frequently have a

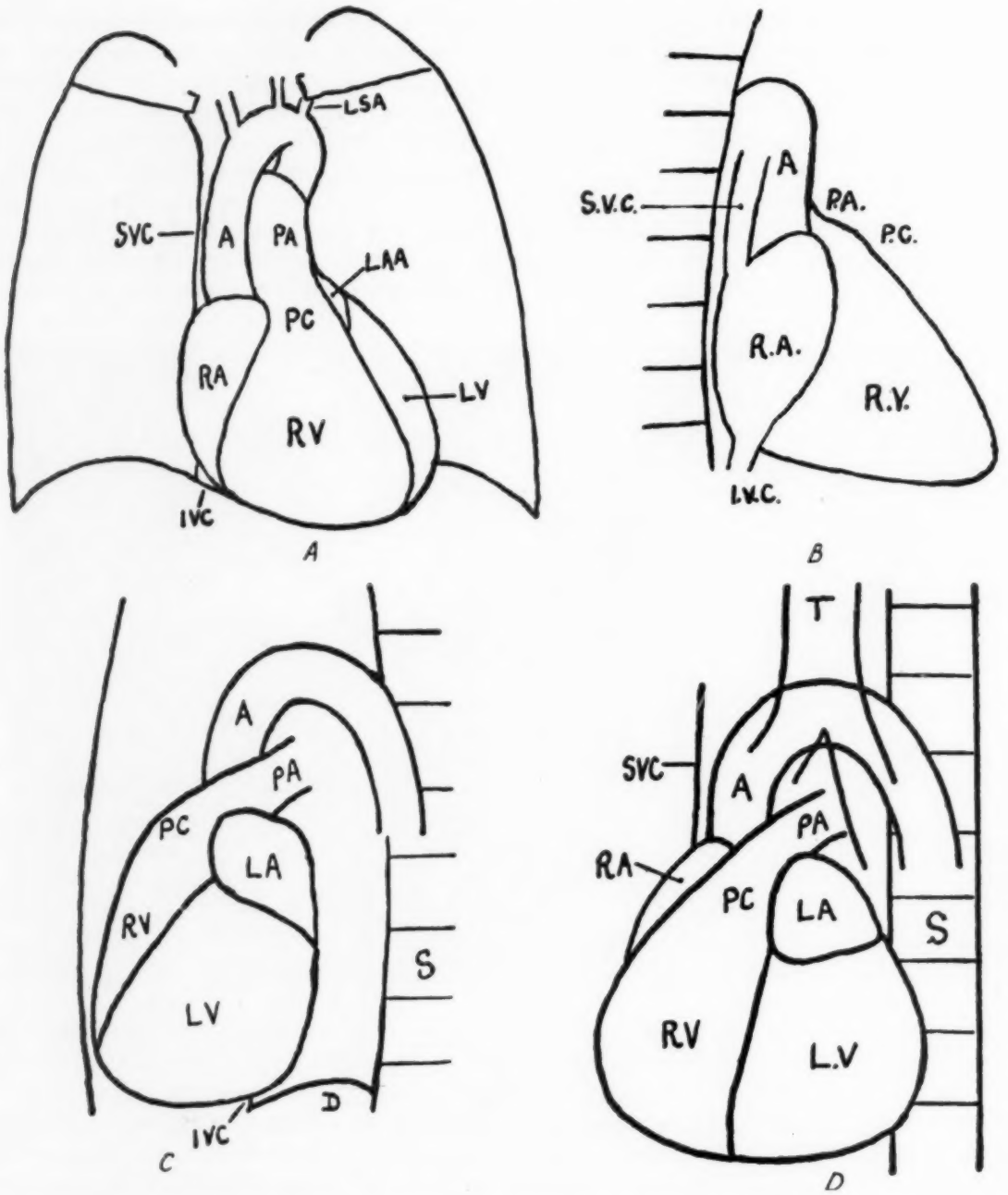

FIG. 7. Topography of heart and great vessels. *T*, trachea; *RA*, right auricle; *PC*, pulmonary conus; *A*, aorta; *LV*, left ventricle; *SVC*, superior vena cava; *RV*, right ventricle; *PA*, pulmonary artery; *LA*, left auricle; *IVC*, inferior vena cava. (Margolies.[19])
A, anteroposterior; *B*, right anterior oblique; *C*, left lateral; *D*, left anterior oblique.

rounded heart than patients with flat chests.[35] In the latter type of patient, the heart has a more oval circumference.

During fetal life, both sides of the heart do about the same amount of work, with the result that, at birth, both sides of the heart are approximately the same size and weight.[10] In some children, the right auricle is dilated at birth, due to the sudden burden of the pulmonary circulation, and

unless the physiological change is recognized as normal, errors in opinions may result. During the first six years, the left ventricle gradually outstrips the growth in the right ventricle until it doubles its thickness and weight. In children between six and twelve years of age, the heart dimensions have been found to be larger in comparison to body weight and size than in adults.[7] As a rule, the dimensions of the female heart are smaller than those in the male of the same age during this six to twelve year period. It has also been demonstrated that the hearts of healthy athletes reach a size which may be considered as a slight cardiac enlargement during periods of training.[35] These same athletes, when examined during a more quiescent period of life, have a decrease in the size of the heart, which then assumes more normal proportions.

Normally, with the patient facing in an anteroposterior direction, the right border of the heart is formed, from above downward, by the right auricle, the inferior vena cava and the cardiophrenic ligament[19] (Fig. 6). In some patients, paracardial fat pads form part of the cardiac border. Roentgenographically, however, the shadow of the outline of the heart may sometimes be seen as a density within the less dense fat pad. The left cardiac border is formed by the pulmonary artery, the left auricle, and the left ventricle.[19] With the patient in the lateral position, the anterior border of the cardiac silhouette is formed, from above downward, by the base of the aorta, the pulmonary conus and the right ventricle (Fig. 7). The posterior border is formed, from above downward, by the arch of the aorta, the pulmonary artery, the left auricle, the left ventricle and the inferior vena cava. The cardiac silhouette, with the patient in the right anterior oblique position, is formed by the right auricle and the inferior vena cava on the right side, with the aorta, the pulmonary artery, the pulmonary conus, and the right ventricle, mentioned in order, from above downward, forming the left border (Fig. 7). With the patient in the left anterior oblique position, the right border is formed by the superior vena cava, the right auricle and the right ventricle, whereas the left border is made up of the silhouette of the aorta, the pulmonary artery, the left auricle and the left ventricle, mentioned in order, from above downward (Fig. 7). These cardiac contours bear a definite relationship both in size and degree of expansion with one another.

Normally, the average anteroposterior diameter of the heart is about two-fifths of the transverse diameter of the chest.[35] While empirical judgment of the size of the heart is used constantly to decide increases in cardiac size, it is by no means satisfactory. The cardiothoracic ratio, diagonal measurements and cardiac area determinations are much more satisfactory. As a rule, however, the average anteroposterior diameter of the heart is less than three-fourths of the average transverse diameter of the heart. Realizing that the average anteroposterior diameter of the heart in females is 8.7 cm. and in males, 7.8 cm., one can obtain a fair impression as to size.[35] The oblique diameter of the heart is about one-third larger than the average anteroposterior diameter.

In the lateral view, the attachment of the pericardium may be seen extending down from the posterior edge of the heart shadow (Fig. 6). It is seen as a faint shadow with its posterior border straight, or slightly concave, extending to the superimposed diaphragmatic shadows. This shadow is a vantage point for observing slight pericardial effusions,[32] which tend to distend the cul-de-sac and distort its normal concave appearance.

During deep inspiration, especially in tall, thin persons, the right and left phrenopericardial ligaments exert a pull upon the domes of the diaphragm, by virtue of their attachments to the diaphragm, which is synchronous with cardiac pulsation. As this frequently occurs in healthy individuals during deep inspiration, it must not be

confused with the abnormal diaphragmatic tug produced by adhesions between the domes of the diaphragm and the pericardium, which may be seen during the expiratory phase of respiration also. Chances for error are minimized by roentgenoscoping patients in the horizontal posture, the patient lying on the right side and the rays projected anteroposteriorly. This allows the mediastinum to drop toward the right, permitting the examiner to see more of the left dome of the diaphragm and its connections with the heart. Phrenopericardial tugging observed in this position may be evidence of adhesions. With the patient lying on one side, the entire mediastinum shifts to the lower side. This evidence can be recorded when the rays are projected in a horizontal plane.[33]

The horizontal position may also be used to advantage in identifying pericardial effusions. One must be well acquainted with the normal appearances of the heart and aorta in this position before using it for refinements in diagnosis. In this position, the transverse diameter of the heart is larger than in the erect position and the width of the shadow of the aorta is greater. This may be due partly to the elevation of the diaphragm. Roesler[37] thinks that there is also an actual increase in the cardiac volume in the horizontal position. Occasionally, a swallow of barium, with the patient in the horizontal position, will outline a cardiac or aortic aneurysmal dilatation, which might otherwise be overlooked.

Under normal conditions, the space between the pericardium and epicardium is very small. It was our good fortune to examine a healthy student with air in the pericardium, as a result of an accidentally inflicted wound. The space between the pericardium and the epicardium, as outlined by air, was almost negligible when compared with the pneumopericardiogram of tuberculous pericarditis.

While practically every portion of the heart may become calcified in disease, the calcification associated with old age must be considered physiological. In the past, roentgenologists constantly overlooked calcifications within the heart.[40] Calcified valves may be seen in the anteroposterior view near the middle or lower half of the heart. The aortic valves are usually seen overlying, or just to the left of, the spine and are therefore more adequately seen on slight rotation. Mitral calcifications, however, lie well to the left of the midline, and when seen in the lateral projection, are situated more posterior than the aortic calcifications. Roentgenoscopically, these shadows have to and fro movements, going toward the apex during systole and returning during diastole.

THE DIAPHRAGM

The right dome of the diaphragm is about 1.5 cm. above the left dome, in most instances. When transposition of the viscera occurs, the opposite obtains. In certain other instances, the shadow of the left dome of the diaphragm is either on the same level or above that of the right dome. We presume that, in the absence of eventration or herniation, such instances may be regarded as normal variants. The splenic flexure of the colon is usually highly placed in such individuals, or there may be a large collection of air in the fundus of a cascade type of stomach, which may be responsible, to some degree, for the position of the diaphragm.

In the anteroposterior and posteroanterior projections, the right and left halves of the diaphragm are dome-shaped. The attachment of the mesial portions of the domes is on a higher level than its attachment to the ribs. This results in a costophrenic sulcus of varying depths. The domes of the diaphragm are regular in this plane and, during inspiration, any peaking may be the result of either pleural adhesions or localized areas of inelasticity of the lung structures. The domes of the diaphragm may be wavy at their outer aspect or produce a shadow of multiple arcs over its surface, due to variation in attachment or hypertrophy of the constituent muscle bundles. This has been de-

scribed as individualization of the costal components. Occasionally, in the postero-anterior and lateral projections, one finds a rounded hump of the mesial aspect of the right dome of the diaphragm. This observation has been reëmphasized[38] as being due in the healthy individual to a weakness of the anteromedial portion of the diaphragm as compared to that of the posterolateral portion. In addition, the inferior vena cava may play a part in preventing downward excursion of the diaphragm. Tumors of the liver and subphrenic lesions may produce an appearance that simulates such a condition.

An anomalous enlargement of the right lobe of the liver will produce a shadow in the lateral view that may simulate that of an interlobar collection.[14] In the lateral view, the domes are higher anteriorly and the posterior costophrenic sulcus is much lower than the anterior, rendering it possible for a relatively large localized pleural collection to escape detection in the dorso-ventral roentgenogram. The upper surface of the shadows of the right and left domes runs from before backward. These shadows may be parallel or may cross each other, either anterior or posterior to a point that corresponds to the middle of the domes. During the inspiratory phase of respiration, the shadows of the domes lose their dome shape and become relatively straight.

The movement of the domes of the diaphragm is extremely variable. The most correct impression of its movement is obtained during ordinary respiration. Frequently, efforts to study diaphragmatic excursion during forced respiration are confusing, due to the influence of costal and abdominal muscles. The movement of the domes of the diaphragm is usually more pronounced in men than in women. The domes are higher and the excursion is greater in the horizontal posture than in the erect. Therefore, anyone interested in detecting slight restriction in movement should examine the patient in the erect posture. This is particularly true in infants and young children. Lateral roentgenoscopy of the diaphragmatic domes, with the patient lying on the back and the rays projected from the opposite side, is difficult because of the increased dome shape of the diaphragm and the encroachment upon the costophrenic sulci. If the patient is studied roentgenoscopically in the horizontal plane while lying on one side, and the rays projected ventrodorsally, the dependent diaphragm will become more cephally placed and will have a greater excursion. These observations have also been noted by Pierson and Newell.[33] Such positions or modifications thereof allow a study of the costophrenic sulci and aid in differentiating between thickened pleura and pleural collections. It must also be borne in mind that diaphragmatic elevation, bilateral or unilateral, is frequently found after abdominal operation, although the patient seems to be perfectly comfortable and normally convalescent.[1]

THE HILUM SHADOWS

The structures in the hila include the bronchi, the pulmonary arteries and veins, the tracheobronchial and aortic lymph nodes, nerves, and connective tissue. The lymph nodes are classified as follows: (*a*) bifurcation nodes, located between the right and left main bronchi; (*b*) tracheobronchial nodes, situated above the bronchi and along the trachea; (*c*) the aortic nodes, and (*d*) the paravertebral nodes. Sukiennikow[41] states that there is a greater number of lymph nodes on the right side. Miller[29] says that there is a greater number of nodes associated with the eparterial bronchus than with the bronchi supplying the middle and lower lobes.

The hilum shadow is irregular in outline with ill-defined borders. The density of these structures, as seen in the roentgenogram, varies considerably with the type of roentgenographic exposure. In the arbitrary properly exposed roentgenogram, the shadow has varying densities and is not homogeneous. It would seem that if roentgenologists could agree upon what a prop-

erly exposed film consists of, varying densities could be regarded as significant observations. We have placed considerable reliance upon individual ability to see varying densities in the hilum shadow, i.e., the bronchial shadow is different from that of the vessels. When the density of the shadow is more or less homogeneous, it is our impression that one can be fairly certain that abnormal changes have become manifest.

The National Tuberculosis Committee[32] has described the limits of the hila as follows:

> On the right side, the normal shadow may be said to extend, from above downward, from the top of the right main bronchus to approximately a point where the right lower-lobe bronchus, below the origin of the middle-lobe trunk, begins to subdivide into its lower-lobe branches (or trunks). This includes the anatomical hilum, the greater portions of the larger bronchi, and some lung tissue in front and behind. The extent of this hilum shadow from above downward is approximately two interspaces and a rib.
>
> On the left side the pulmonary artery passes above the left bronchus, and from above downward the left hilum shadow may be said to extend from the upper border of the pulmonary artery down to approximately a point where the left lower-lobe bronchus begins to subdivide into its lower-lobe branches (or trunks). Such a hilum shadow on this side is slightly shorter than the one on the right and is slightly less than two interspaces and one rib in length.
>
> While the top of the right bronchus is higher than the left, if the tops of the hilum shadows be limited in the manner just described they are on a plane approximately level.
>
> The thickness of the hilum shadow in the anteroposterior direction is a matter that requires further study, and probably largely from the lateral view. Measurements from lateral views are very uncertain and subject to considerable personal equation. One should learn to acquire the idea of depth as well as length and width when interpreting hilum shadows.

In the lateral view, the shadows of the hila are superimposed and it is impossible to define their limits, even within wide margins, because of so many variable factors, such as target film distance, length of time of exposure, and disturbed shadow outline due to transmitted pulsation from adjacent vessels. We suggest, however, that one can develop an individual impression as to their normal extent by studying roentgenograms of the chests of healthy individuals, made with a Potter-Bucky diaphragm in an almost lateral projection, with the patient so placed as to prevent the superimposition of the hila. Such films allow one to see shadows of the varying densities of the hila, and, if a thorough understanding is obtained, it becomes possible to determine deviations from the normal with a high degree of precision.

In the dorsoventral and ventrodorsal roentgenograms, the outer boundary is regarded as normal when it lies within the inner zone of the lung field. Everyone familiar with the interpretation of variations of hilum shadows realizes how difficult it may be. Oblique and lateral views often assist in detecting glandular enlargements that might otherwise escape notice.

Calcified lymph nodes occur frequently in the hila of healthy individuals. They represent, as a rule, evidence of a preexisting active tuberculous process. Calcification of a lymph node does not necessarily mean that the node may not contain viable tubercle bacilli which, under certain conditions, are capable of multiplying and setting up an active disease. In adults, we have felt that nodes that are calcified in a relatively homogeneous manner are probably healed, whereas those in which the calcification is punctate and appears as a mottled shadow have a much greater potentiality for reactivation. Chests of children with calcified nodes of this type should probably not be regarded as healthy. While it is true that calcified nodes are usually regarded as evidence of past tuberculous infection, it is entirely possible for them to be due to some other process.

It is important to evaluate the dense, circular shadows, due to vascular trunks obtained in an axial plane, and appearing

in the roentgenogram as densities similar to those cast by calcified nodes. These shadows are readily seen roentgenoscopically and, should any doubt arise as to their nature, slight rotation of the patient will permit identification of their true nature. Calcified shadow densities do not disappear on rotation, whereas vascular shadows do.

THE ZONES

The chest has been variously divided into different zones for convenience of description of the single film. The classification in most frequent use is that which divides the one side of the thoracic cavity into three zones: the inner or hilum, the middle or truncal (or vascular markings), and the peripheral, which contains the finer subdivisions of the vascular tree in which the only shadows visible consist of fine linear markings (Fig. 6).

In stereoscopic films, there is very little occasion to use such a classification, except so far as the various zones have different capacities for expansion.[12] The hilum zone expands and contracts less than the truncal or vascular zone, and the peripheral zone has more expansile and contractile power than the truncal or vascular zone.

THE LOBES

Ordinarily, the right lung is divided into three lobes and the left, into two. Not infrequently, there is an accessory lobe on the right side called the azygos lobe.[42] This lobe is recognized by the fine pleural line which extends from the apex of the lung downward, to end as a dense oval shadow near the upper aspect of the right border of the superior mediastinum. The dense oval shadow is due to the azygos vein, which maintains its fetal position and carries with it a reflection of the parietal pleura, down to the point of entrance into the superior vena cava. The size of the azygos lobe is quite variable, depending upon the position of the vein (Fig. 2).

More recently, other accessory lobes have been described in roentgenologic literature.[34] An accessory lobe may occasionally be found at the base of either lung, either partially or completely formed. These lobes are variable in size and represent a division of the lower lobe. They can be recognized by the presence of interlobar pleural shadows, extending upward from the mesial portion of the domes of the diaphragm toward the hila. This lobe may occasionally be the site of a pathological process and therefore readily recognizable. On one occasion, we observed two lobes only, on the right side. The observation was later confirmed by post-mortem examination.

The position of the various lobes is readily observed in those instances where either interlobar shadows are visible or after introduction of an opaque medium into the bronchi. It should be emphasized, however, that the size and extent of the lobes are quite variable. On occasions, the lower lobes may extend very high posteriorly, so high that physical signs, and even shadows in the roentgenogram, may be misinterpreted as representing lesions in the lower portion of the upper lobe.

THE VASCULAR MARKINGS

Extending from the hilum on either side are heavy shadows passing into each lobe. These shadows are more pronounced in the lower lobes and, in roentgenologic literature, are described as truncal shadows. It has seemed to us, however, that such a terminology conveys an impression that a bronchus is responbible for, or at least associated with, these visible shadows. From the work of Miller,[22] Miller,[23,24,25,26,29] and Greineder,[9] such an interpretation may not be true. For years, roentgenologists attempted to localize foreign bodies and pathological lesions according to the distribution of these shadows as they passed into each lobe. It was recognized that only very large bronchi were visible, and these were restricted, for the most part, to the hilum zone. On the other hand, the roentgenologist thought that the truncal shadow, as seen and de-

scribed in the roentgenogram, consisted of bronchus, artery, vein, nerves, lymphatics, and connective tissue. Wherever one of the large branch shadows was seen, there was thought to be a bronchus. We know now that such is not the case. Miller[24] has shown that "the pulmonary artery follows, in all of its subdivisions, the subdivisions of the bronchial tree. As each main branch of the pulmonary artery arches over its corresponding stem bronchus, it comes to occupy a position posterior (dorsal) and slightly lateral to the bronchus. The relation of the main trunks of the pulmonary vein to the bronchi is quite different; they are situated anterior (ventral) and mesial to their stem bronchi and in their ultimate distribution are situated as far removed from bronchi as possible."

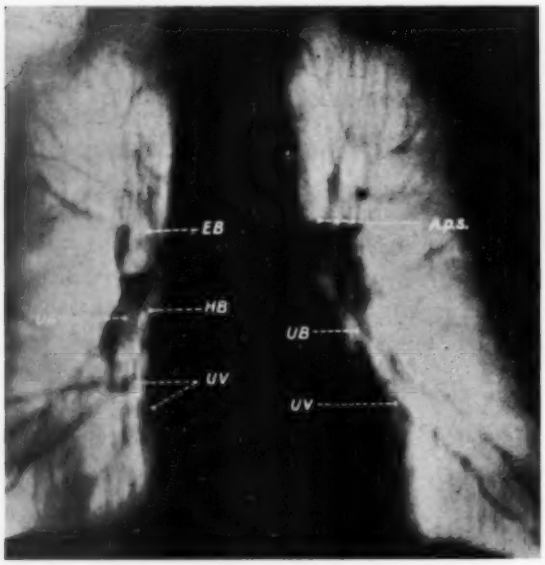

FIG. 8. Tomographic presentation of vascular markings. *EB*, eparterial bronchus; *HB*, lower lobe bronchus; *UA*, lower lobe artery; *UV*, lower lobe vein. Note distance between artery and vein. (Greineder.[9])

Miller,[22] interested in another phase of the same subject, made similar observations, as did Greineder,[9] with even more striking demonstrations by tomography (Fig. 8). If one can be certain that veins, as a rule, have a larger diameter than the arteries, it is our belief that the shadows of the larger veins can be differentiated from the larger arteries in roentgenograms of excellent detail made during the diastolic phase of the cardiac cycle.

We appreciate that the above discussion may be considered academic and of no practical importance so far as the distribution of the bronchi is concerned, because of the improved methods for delineating bronchi after the instillation of opaque media and the increased use of the bronchoscope. Nevertheless, it is our firm belief that too many roentgenologists are misinterpreting normal variations of the vascular markings in terms of pathology. Miller,[24] in 1919, recognized and warned us of such a possibility. Now, it has become necessary for industry to have pre-employment as well as follow-up examinations and, unfortunately, many roentgenologists, upon whom the burden of the roentgen examination has fallen, are, *all too frequently, misinterpreting vascular shadows as fibrosis, and thereby imposing an unnecessary hardship on both the employee and the employer. It is time that we familiarize ourselves with normal appearances. We have an obligation to fulfill and should be worthy of the responsibility and opportunity afforded us.*

Vascular shadows are otherwise confusing in interpretation, particularly with regard to the dense, circular shadows, due to blood vessels recorded in an axial plane, which may simulate an appearance of thoracic calcium[22] and, in the more peripheral portions of this zone, may produce an appearance of beading or early nodulation, when the roentgenogram is made during the systolic phase of the cardiac cycle. The appearance of beading may simulate that of a pathological process, such as that seen in silicosis, baritosis, or a mycotic infection. Stereoscopic dorsoventral films may not be sufficient to identify the exact nature of the shadows, but films exposed in an oblique view and rotation of the patient during the roentgenoscopic examination will usually be of

aid. If the dense shadow is due to a blood vessel, slight rotation will cause the shadow to disappear; if due to a calcified lesion, the shadow will remain. Furthermore, the blood vessel shadows are circular and homogeneous, whereas a calcified lesion may be irregular and less homogeneous, or even mottled (Fig. 9).

investigation is necessary. This work, thus far, serves to show that vascular displacement and vibration cause considerable blurring of roentgenographic detail. Likewise, kymograms illustrate clearly what a marked influence the cardiac pulsation exerts on the lung structures close to the heart.

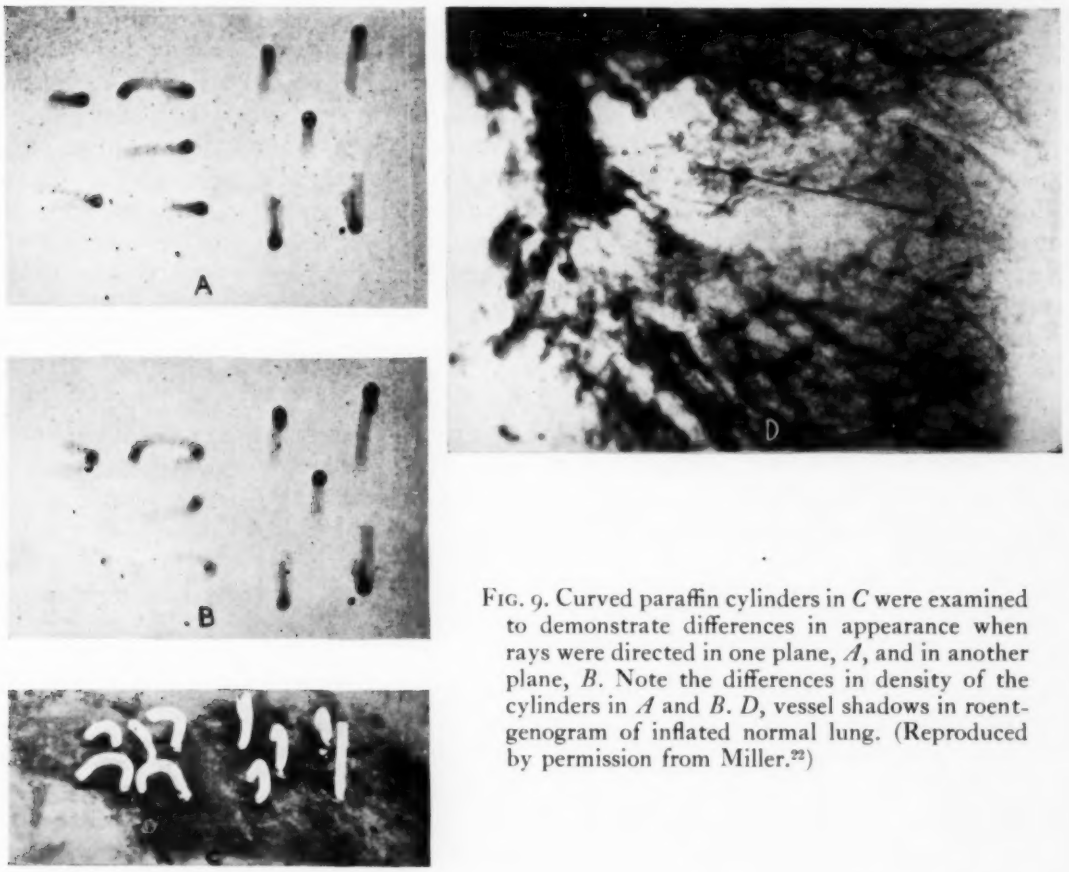

Fig. 9. Curved paraffin cylinders in *C* were examined to demonstrate differences in appearance when rays were directed in one plane, *A*, and in another plane, *B*. Note the differences in density of the cylinders in *A* and *B*. *D*, vessel shadows in roentgenogram of inflated normal lung. (Reproduced by permission from Miller.[22])

Miller[29] called attention to another structure, the ring-shaped cartilage which occurs where bronchi leave the main stem bronchi. This cartilage may produce a dense, circular shadow in the roentgenogram.

McPhedran and Weyl[20,21] have emphasized the importance of synchronizing the roentgen exposures of the chest during the late diastolic phase of the cardiac cycle. They have performed important experiments in an effort to evaluate this phase of the general problem, but further

THE BRONCHI

The first subdivision of the right bronchus is the *right upper lobe bronchus* (eparterial), which comes off at an angle of almost 90 degrees and passes above the pulmonary artery. This bronchus gives off a branch, the vertebral, which passes upward to the apex of the lung parallel to the spine. This bronchus gives off branches which extend anteriorly and posteriorly. The upper lobe bronchus gives off another important branch which is designated as the second interspace bronchus, because it comes off

behind the level of the second interspace in front. Likewise, this bronchus gives off anterior and posterior branches.

The portion of the right bronchus between points from which the upper and middle lobe bronchi come off is termed the *stem bronchus*. Foreign bodies frequently lodge in this region.

The *middle lobe bronchus* comes off the stem bronchus anteriorly. It divides into many branches, but there are two main divisions, as a rule: (*a*) the branch which passes downward and anteriorly, and (*b*) the branch that passes upward and laterally.

The *lower lobe bronchus* bifurcates into several main branches which have been variously described as the anterior, middle, posterior division branches in the lower portion of the lower lobe, and the apical branch in the upper portion. All of the main subdivisions give off many branches. Disease of the mesial and posterior division bronchi produce shadows that border upon the shadow of the heart in dorsoventral roentgenograms. Further identification of the bronchi can be obtained in the oblique and lateral projections.

The *left upper lobe bronchus* (hyparterial) passes below the pulmonary artery. Its subdivisions are similar to those of the right side, except that there is a branch which goes to the lingual tip of the upper lobe which is that portion in front of the heart.

The *left lower lobe bronchus* has a longer course than that of the right side before it gives off any subdivisions, otherwise it and its subdivisions are similar to those of the right side.

THE LUNG FIELDS

Medicine owes a debt of gratitude to William Snow Miller whose life has been dedicated to the study of the anatomy of the lung. No discussion of the healthy lung can possibly be complete without frequent reference to Miller's work, and much of that which we shall discuss has been gleaned from his reprints and recent book.[29]

In the discussion of the healthy lung, we have approached its consideration from the standpoint of the smallest functioning unit in the lung, the primary lobule. It is obvious, therefore, that the following discussion is of more importance histologically than roentgenologically.

As the bronchial tree is followed to its ultimate divisions, there occurs a lack of the regular bronchial outline and the gradual appearance of an air passage, whose walls are lined with variable, irregularly placed air spaces. These terminal air channels are called the respiratory bronchioles, which, in turn, divide into smaller branches known as the alveolar ducts. These alveolar ducts are smaller than the respiratory bronchiole from which they spring and are lined by more alveoli than the aforementioned bronchiole.[23,25] The alveolar ducts, in turn, lead into from two to five spheroidal cavities called atria. The atria, in turn, open into numerous air sacs around the periphery of which are situated the alveoli.

The bronchial musculature forms sphincters about the channels leading into the atria and around the alveoli which line the smaller bronchioles.[26] These sphincters probably play an important rôle in the muscular spasm known to occur in asthma. Normally, air passes unimpeded by these sphincters. With muscle contraction, the air channels reduce in size preventing the egress of air, which produces an increase in residual air with the formation of emphysematous lobules.

The structures described above comprise the anatomical unit or primary lobule of the lung, which may be defined as a ductulus alveolaris, the air spaces connected with it, and all their associated vessels, nerves and lymphatics. The primary lobule has the form of a truncated pyramid, with its base directed toward the periphery of the lung.[23,25] Its air passage (ductulus alveolaris) usually enters the primary lobule at the side rather than at its apex. Primary lobules vary in size from

0.45 mm. to 0.845 mm., the larger units situated in the peripheral and basilar portions of the lung. It is obvious that these lobules are not seen in the roentgenogram. It is only barely possible that one sees, roentgenographically, the larger, secondary lobules, which are made up of 50 to 250 of these primary units.

The primary lobules receive relatively little blood from the bronchial blood vessels.[23,25] The pulmonary artery, on the other hand, follows the course of the respiratory bronchiole and the alveolar duct into the center of the primary lobule[3] (Fig. 10). Each atrium is supplied by a branch of the pulmonary artery, which then divides into enough smaller tributaries to supply the alveolar sacs. The pulmonary vein, in contradistinction to the pulmonary artery, courses along the periphery of the primary lobule at a distance from the air channels[3] (Fig. 10). Its branches arise from the pleura, the end of the alveolar duct, the walls of the alveolar sacs and the points of division of the bronchi and bronchioles.

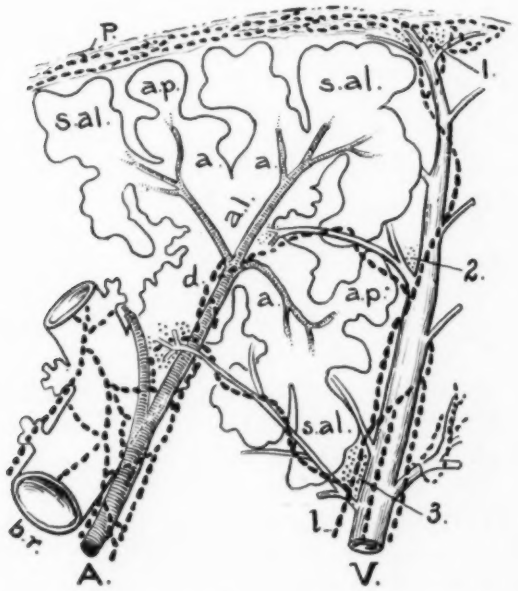

Fig. 10. Primary lobule. *s. al.*, sacculi alveolares; *a.p.*, alveoli pulmonum; *a.*, atria; *d.al.*, ductuli alveolares; *b.r.*, bronchiolus respiratorius; *A.*, pulmonary artery; *V.*, pulmonary vein; *P.*, pleura. The dotted lines are the lymphatic vessels; *1*, *2* and *3* are lymphoid deposits. (Reproduced by permission from W. S. Miller.)

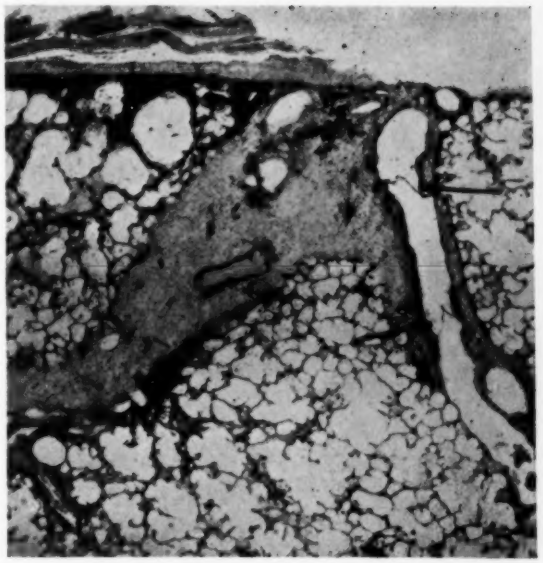

Fig. 11. Valves in a lymphatic vessel near the pleura. (Reproduced by permission from Miller.[25])

The lymphatics of the lung may be divided into the deep lymphatics and the superficial lymphatics.[25] The deep lymphatics include all of the channels which follow the bronchial tree and its associated blood vessels toward the hilum. The superficial lymphatics lie within the pleura.

The bronchial lymphatics in the primary lobule are three in number, with no lymphatics present in the air spaces as vessels (Fig. 10). The lymphatics of the pulmonary artery lie between the artery and the bronchiole, anastomosing with one of the three bronchial lymphatics. These, in turn, unite with others to form a rich network running toward the hilum. The lymphatics of the pulmonary veins follow the course of the veins from the various points of origin described previously, with one exception. Since no lymphatics lie in the walls of the air sacs, there are no lymphatics along the veins arising from their walls.

The pleural lymphatics form a rich network which drains into the lymph nodes in the hilum. There is some evidence

supporting the belief that the superficial pleural lymphatics, covering the diaphragmatic surface of the lower lobes, drain into the abdominal pre-aortic nodes by way of the ligamentum pulmonale.[25] The numerous valves in the superficial lymphatics point in no particular direction. The valves are less numerous in the deep lymphatics and lie close to the hilum in the large vessels, allowing flow in the direction of the hilum only. Similar valves lie in some of the deep lymphatics close to the pleura. These valves point toward the pleura, allowing lymph flow into the superficial pleural lymphatics without permitting a reflux of superficial lymph into the deep set of lymphatics (Fig. 11).

In addition to the lymph vessels, the primary lobule contains small masses of lymphoid tissues, which may be found in the walls of the primary lobule.[28] Besides these distinct lymphoid masses, one can identify a sheath-like dispersion of lymphoid tissue along the pulmonary artery and along the air channels. This faintly defined sheath of lymphoid tissue is rarely found in the lungs of humans under thirty years of age. With the advent of middle life, however, these lymphoid deposits become more conspicuous until they are quite prominent at approximately sixty years of age. The lungs in healthy individuals over sixty frequently show the artery and bronchus completely surrounded by this lymphoid tissue.[28] Perhaps this accounts for the prominent linear markings frequently associated with advancing age, markings which are usually lacking in children and young adults. It is important to know the distribution of these lymphatic masses and lymphoid networks as they are the centers about which disease processes often commence.

Considerable evidence has been accumulated substantiating the belief that massage, passive motion, capillary wall injury, increased venous and capillary pressure, and decreased blood proteins accelerate lymphatic flow.[6,11] The importance of these findings may be appreciated when one realizes that the rate of lymph flow and the progress of phagocytes within lymph vessels are negligible when the part being studied is at rest. Without the former observations, one would be at loss to explain the rapid appearance in the hilum glands of foreign particles dusted into the lung. In one set of experiments, ink particles were demonstrated within the hilum nodes several minutes after their injection into the lung.[6] Drinker and Field[6] demonstrated that phagocytosis was not entirely responsible for the transfer of foreign particles into the perialveolar spaces. Perhaps alveolar pores really do exist, allowing free interchange of such material.[27,18] This, in part, helps explain the rapid appearance of foreign bodies in the hilum nodes, as the finding obviates complete dependency upon phagocytosis in the transfer of foreign material from the alveolus into the perialveolar tissue.

Dolley and Wiese[5] recently found that unilateral pneumothorax produced a decrease of about 45 per cent in the lymph flow from the lungs. Such data, correlated with those previously referred to, would seem to indicate that the respiratory excursions of the lungs and the massaging action of the pleura play an important rôle in pulmonary lymph flow. It also seems reasonable to conclude that the rate of lymph flow might vary in different portions of the lung, depending upon differences in respiratory excursion in various portions of the lung. That such differences in the amplitude of pulmonary expansion do occur seems well substantiated by the work of Keith, Miller, Scott, et al.

While there is good evidence indicating that lymph constantly courses through the lung toward the hila, no absolute proof concerning the magnitude of this lymph flow is available. Drinker and Field[6] were unable to demonstrate any appreciable flow in their animal experiments. If little is known concerning this particular factor, certainly less is known of the true function of the lymphatics.

Effect of the Phases of Respiration on the Roentgen Appearances in the Chest

During inspiration, the first five ribs rotate up and out, carrying the sternum forward and upward (Fig. 12). These movements increase the anteroposterior dimensions of the chest, thereby expanding the upper lobe in an anteroposterior direction, allowing an influx of air.[12] The ribs main-

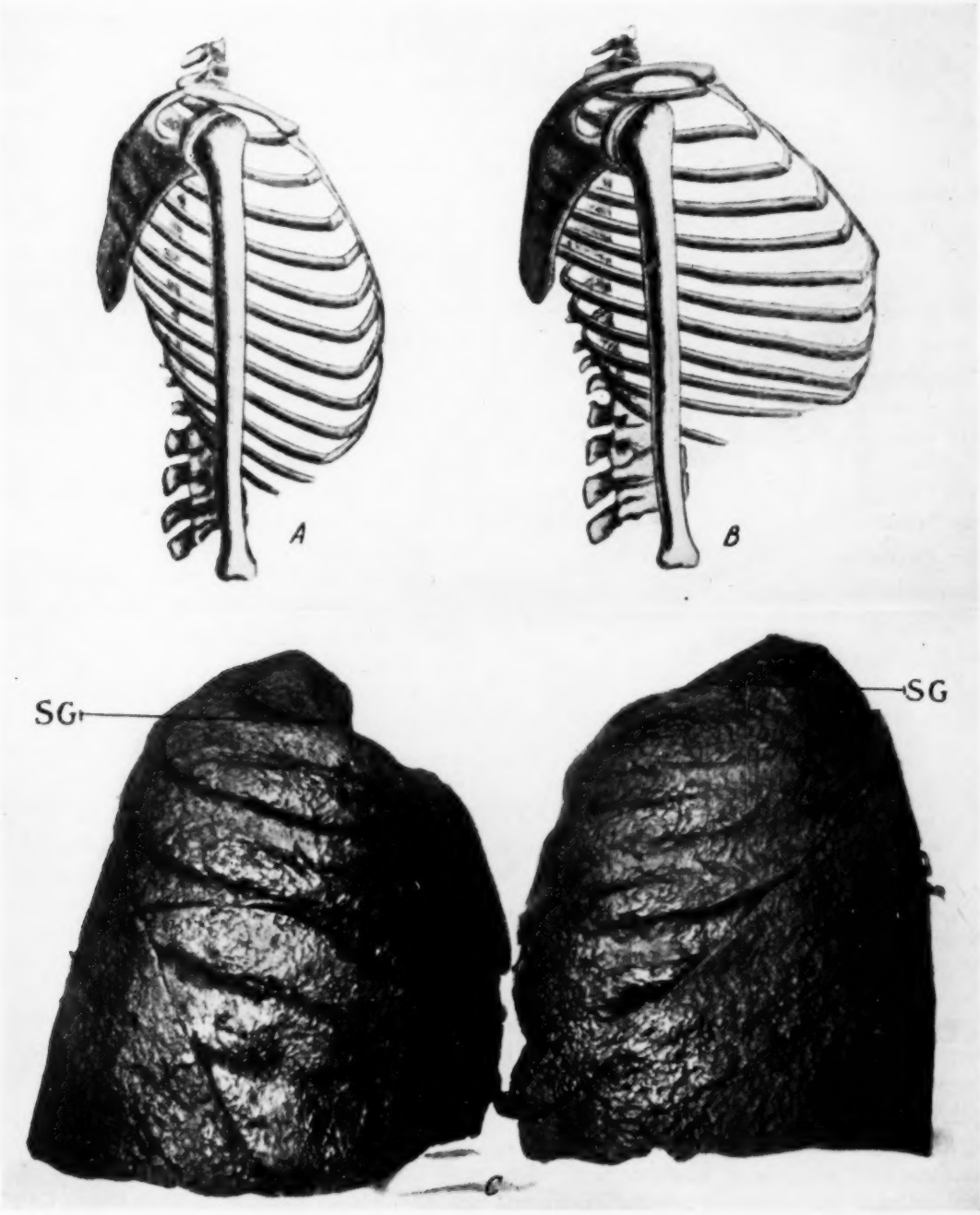

Fig. 12. Thoracic cage in expiration, *A*, and inspiration, *B*. Note how the upper ribs carry the sternum forward and up. *C*, hardened lungs showing rib markings. (Reproduced by permission from Norris and Landis. Diseases of the Chest, 1917, pp. 24; 74.) (Courtesy W. B. Saunders Co., Philadelphia.)

tain a constant relationship with the upper lobe in its anteroposterior excursions, with the result that the impressions of the first five ribs may frequently be seen in postmortem specimens on the anterior surface of the upper lobe (Fig. 12). Such markings,

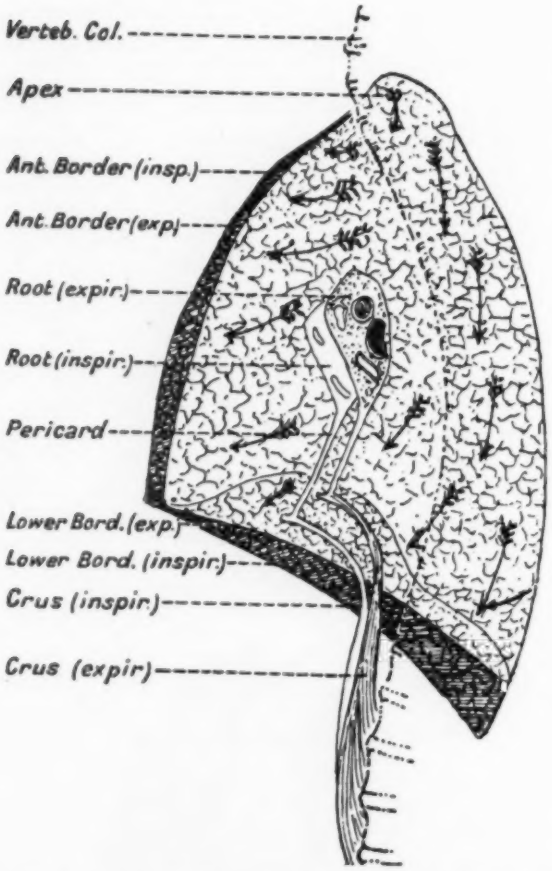

Fig. 13. Diagram showing how the lung expands as the result of the various respiratory forces. The entire lung expands in a forward and downward direction. (Keith.[12])

however, are unusual in the lower lobes. During inspiration, the lower lobes are expanded by the descent of the powerful diaphragmatic muscles, which increase the depth of the chest, and by the action of the lower intercostal muscles, which increases the transverse diameter of the chest.[12] These forces are much greater than those influencing the upper lobes. Because of this, the lower lobes are drawn downward during inspiration, thereby massaging its pleural surfaces against the long axis of the ribs, which explains the absence of the rib markings previously referred to as being commonly found in the upper lobes (Fig. 12). The evidence concerning the formation of rib impressions in the upper lobe is indirect. Clark[3] has called our attention to the relative lack of pigmentation of the lung surface where rib impressions are found, whereas more pigmentation is found in the lung tissue adjacent to the intercostal muscles. Such evidence is in favor of Keith's[12] ideas concerning the mechanism of respiration. Clark[3] also believes that these observations support the premise that the massage effect of the ribs is an important factor in lymphatic flow. This seems reasonable in view of the fact that other portions of the lung, such as the lung around the heart, the tip of the lung extending into the costophrenic sulcus (where it is massaged by the diaphragm), and the posterior surfaces of the lower lobes, are less pigmented than the inside of the lung and the lung surfaces where massaging action is minimal. The summation of these inspiratory forces produces expansion in a forward, downward and outward direction, with considerably more expansion taking place in the lower lobes than in the upper[12] (Fig. 13). The trachea and its ramifications also feel the effects of these inspiratory forces as the trachea and hila move downward and forward, while the bronchial tree and the vascular structures become elongated.*[16,17] Keith[12] has stated that, when more is learned about normal respiration, the lobation of the lung and the great fissures will be found to be of functional significance.

Working against these inspiratory mechanisms are the heart, the vertebral column and vertebral portions of the ribs. These portions of the chest are antagonists to pulmonary expansion by virtue of their anatomical characteristics.[12,16,17] Being relatively fixed structures, they cannot move

* Keith and Miller believe that the bronchial tree spreads and elongates during inspiration. Macklin's work, while not conclusive, does not support the spreading of the bronchi, although it does show the elongation very well (Fig. 15).

to allow the nearby lung to expand (Fig. 14).

In like fashion, the apex of the upper lobe does not expand as fully as the lower portion of the upper lobe, which is not inhibited by the peculiar conical shape of the upper thoracic cage (Fig. 14). One can conclude, therefore, that the amount of air entering the lower lung field and periphery of the lung is greater than that which enters the upper lobes or hila.

Before concluding this discussion, attention should again be directed to the importance of respiratory movements upon the lymphatic flow and its possible influence upon the distribution of a pathological process. While the evidence is purely deductive, it seems reasonable that adequacy of lymphatic flow and degree of respiratory mobility go hand in hand. Perhaps this might account for the frequency of upper lobe tuberculosis and for the mid-lung field changes of silicosis. Perhaps it might also account for the clear peripheral and paracardiac zones in the lung fields in patients with pronounced changes due to silicosis with a quiescent infection.

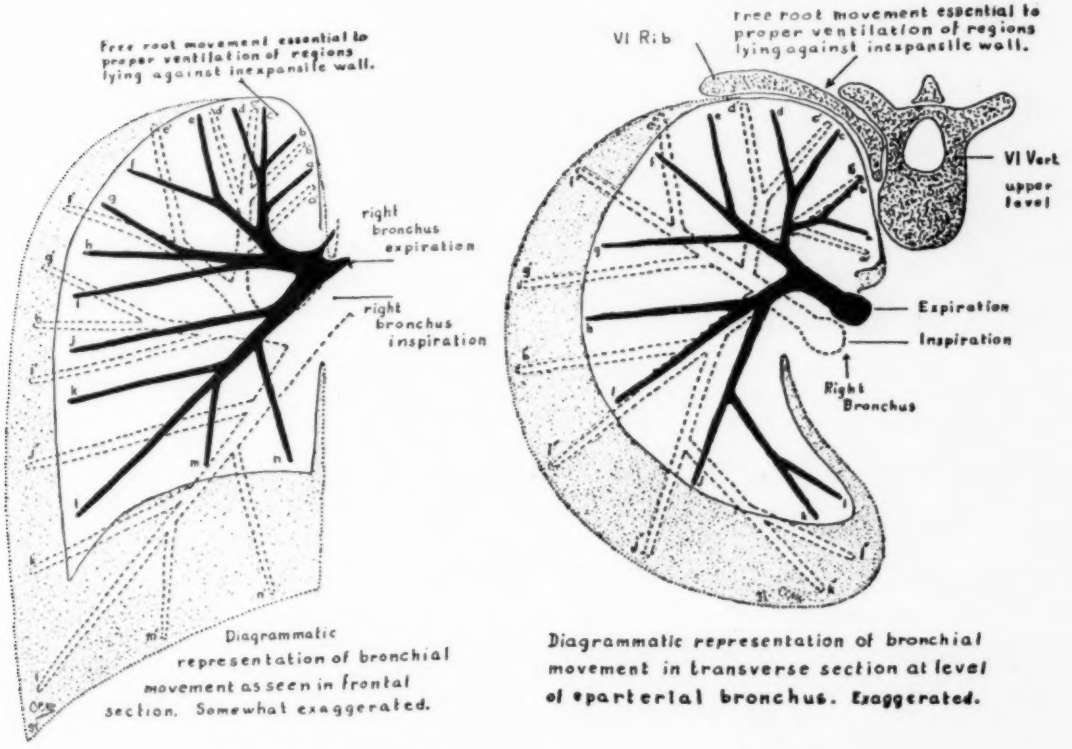
Free root movement essential to proper ventilation of regions lying against inexpansile wall.
right bronchus expiration
right bronchus inspiration
Diagrammatic representation of bronchial movement as seen in frontal section. Somewhat exaggerated.
VI Rib
Free root movement essential to proper ventilation of regions lying against inexpansile wall.
VI Vert. upper level
Expiration
Inspiration
Right Bronchus
Diagrammatic representation of bronchial movement in transverse section at level of eparterial bronchus. Exaggerated.

Fig. 14. Diagrams showing the differences in expansion in the various portions of the lung. Note decreased expansion in upper lobe and in paravertebral gutter. (Reproduced by permission from Macklin.[17])

ROENTGEN TECHNIQUE

The importance of roentgenoscopy in examination of the chest cannot be overemphasized, provided the eyes are accommodated. In addition to the usual roentgenoscopic observations, one can, by this method, determine the positions, and the types of exposures necessary to reveal the most information roentgenographically. Esophageal studies are too frequently neglected and should be included in chest roentgenoscopy, especially in those patients who complain of either shoulder or substernal pain. Oftentimes, the finding of a large diverticulum or adhesion of the esophagus will explain the cause of marked

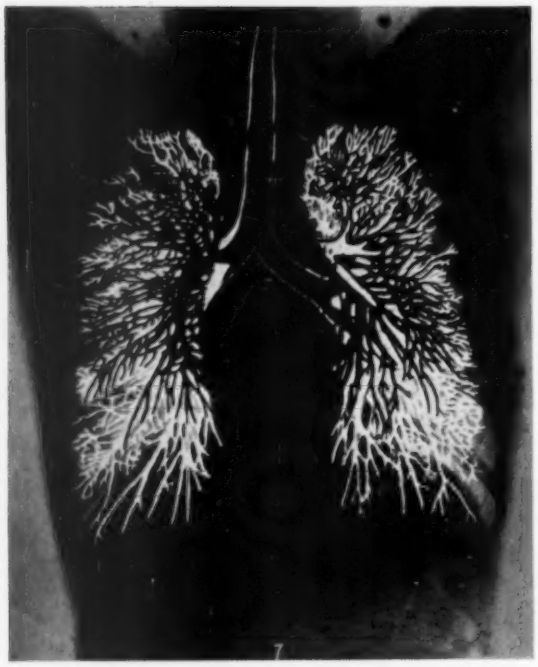

FIG. 15. Composite drawing demonstrating bronchial elongation during inspiration. (Reproduced by permission from Macklin.[16])

lung changes in the patient, who is unaware that he is aspirating esophageal contents into his trachea.

Considerable data have been accumulated showing that the diagnostic value of chest roentgenograms depends upon certain film characteristics which are determined by the technical factors used for the examination.[43,44] For this reason, certain fundamental technical requirements have been defined which, when adhered to, have produced a high quality of chest examination. Briefly, these factors may be summarized as follows:

1. *Time.* Exposures made in from 1/30 to 1/10 second are essential to overcome lack of detail resulting from vascular motion. Synchronization of the roentgenographic exposures with the late diastolic phase of the cardiac cycle further reduces vascular blurring. This method, if coupled with some means of determining full inspiration, would be ideal, as one could then be reasonably sure that slight vascular changes in different films of the same patient were, or were not, due to physiological variations.[20,21]

2. *Distance.* Focal-spot film distances between 4 and 6 feet are most satisfactory, as distances under 4 feet produce considerable distortion, while exposures made at distances over 6 feet are not sufficiently

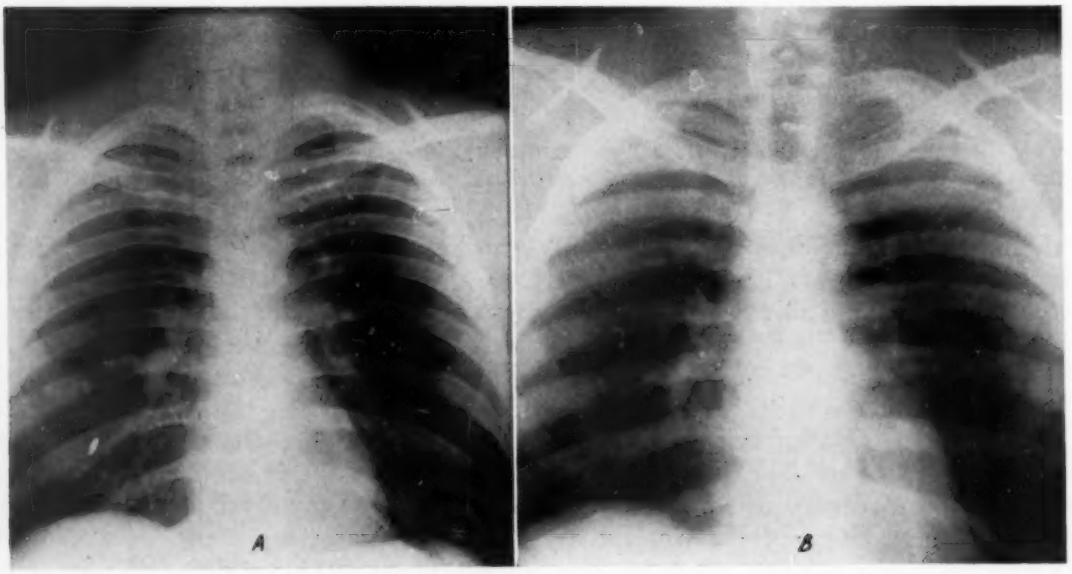

Fig. 16. *A*, healthy chest; *B*, second film of stereoscopic pair showing marked changes which are the result of over-developing in an impure solution.

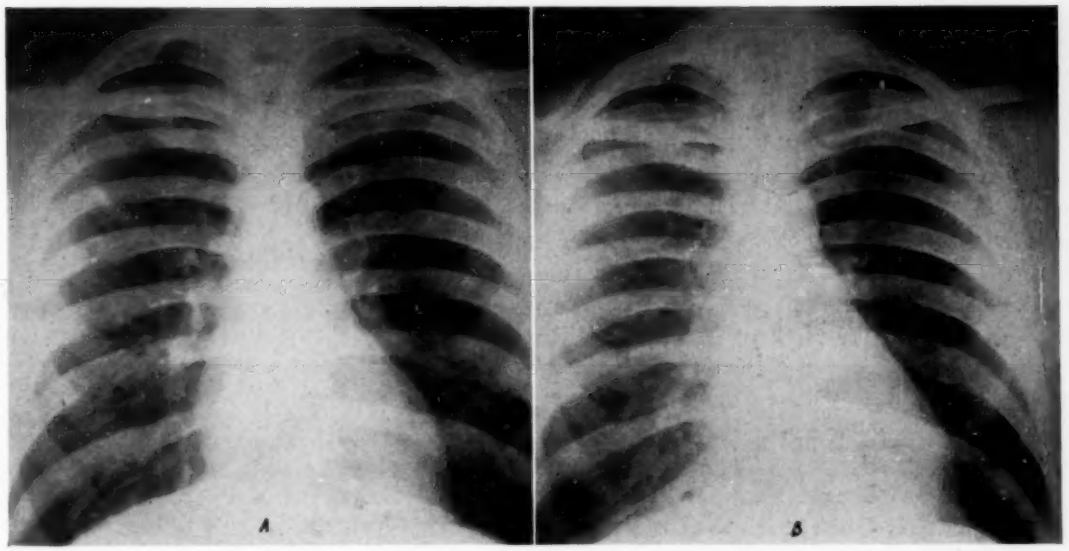

Fig. 17. *A*, healthy chest; *B*, same patient. Note the increased density over the right hemithorax which is due to slight rotation. This was produced by the supporting strap when the patient was placed against the film changer.

superior to warrant the expense of bulky high tension apparatus.

3. *Screens.* Screens should be chosen for excellence of detail, although high-speed intensifying screens are of considerable assistance in avoiding blurred images. Screens must be kept clean and care taken that contact is maintained throughout their surfaces.

4. *Voltage.* The roentgen tube voltage should be so chosen that the densities in the diagnostic areas of the film will lie between the limits of 0.4 and 0.6. This depends upon the other physical factors employed, but, as a rule, will vary from 50 to 80 kv. (peak).

5. *Current.* The choice of the tube current also depends upon each of the factors previously considered. Bearing these factors in mind, that tube current should be chosen which will produce proper roentgenographic densities.

6. *The Roentgen Tube.* The line or band focus tubes have been recommended as they combine the detail produced by a small effective focal-spot with the durability of the broad focal-spot tube.

7. *Film Processing.* Unless a time-temperature method of development is employed, in which all factors are carefully calibrated and controlled, it is useless to follow the technique described. Warm solutions, impure chemicals, over or under developing will ruin any film, no matter how perfect its exposure may have been (Fig. 16).

In addition to these factors, it is necessary to use accurate methods for measuring patients. One must also be careful to make all measurements through the same anatomical points. An impulse timer, a cathode current stabilizer, suitable indicating meters, adequate power supply, full wave rectification for the high tension equipment, and 1 kv. per step autotransformer control, are all essential for obtaining roentgenographic results which can be repeated on different occasions.

Stereoscopic examinations made in the anteroposterior or posteroanterior directions are desirable in chest roentgenography. The gross exaggeration of vascular markings and other abnormal densities, seen in single flat films of the chest, is avoided and properly evaluated by stereoscopy, which places these questionable areas at their right depth. Lateral, oblique, recumbent, or any other position, deter-

mined roentgenoscopically, will add valuable information.

Most chest cassette changers are equipped with some type of fixation device, such as a windlass and binder, which encircles the patient's back for immobilization. After immobilization has been accomplished, care must be exercised to determine whether or not the patient is rotated. Even slight rotation will cause a difference in density of the two sides of the chest. Such differences in density have been regarded, by some, as evidence of pleural thickening or hypoventilation (Fig. 17).

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THE RIGHT OBLIQUE HORIZONTAL (SUPINE) POSITION IN THE DEMONSTRATION OF THE DUODENAL ULCER CRATER

PRELIMINARY REPORT

By EDWARD SCHONS, M.D.
ST. PAUL, MINNESOTA

THE orthodox methods in the roentgenological examination of the stomach and duodenum with the opaque meal have for many years consisted primarily of roentgenoscopy, with the aid of manual palpation and manipulation at various angles in the erect posture. This method, at the hands of a skilled roentgenoscopist, is sufficient in many cases for eliciting evidence of, or ruling out, gastric and duodenal disease, including the duodenal ulcer crater. The roentgenoscopic examination in the erect position is, however, usually followed by roentgenoscopy in the horizontal posture, the usual sequence being examination in the supine, or recumbent position, the left oblique and left lateral recumbent, the prone, the right oblique prone and right lateral prone positions. Roentgenograms are usually made in one or several of these positions.

Of the horizontal positions, both in roentgenoscopy and roentgenography, the recumbent and the left oblique and left lateral recumbent or supine positions, with or without the Trendelenburg tilt, have been chiefly of value in the demonstration of abnormalities and pathological conditions of the cardiac third of the stomach, while the prone position, through all angles to the right lateral horizontal position, has been most useful in the examination of the pyloric two-thirds and duodenum. For roentgenographic purposes the tube in all these positions is usually over, and the film under, the patient. The majority of roentgenologists have combined the roentgenoscopic and roentgenographic methods, many favoring relatively more either the one or the other method. Both methods have sufficed very well to bring out deformities and filling defects in the outlines of the stomach and cap, including the demonstration of ulcer craters which can be brought into profile at the available angles at which the stomach and cap can be viewed. Palpation under the screen, usually in the erect position, has brought into view many ulcer craters, both of the stomach and cap, not otherwise clearly demonstrable. This method has been for years very successful

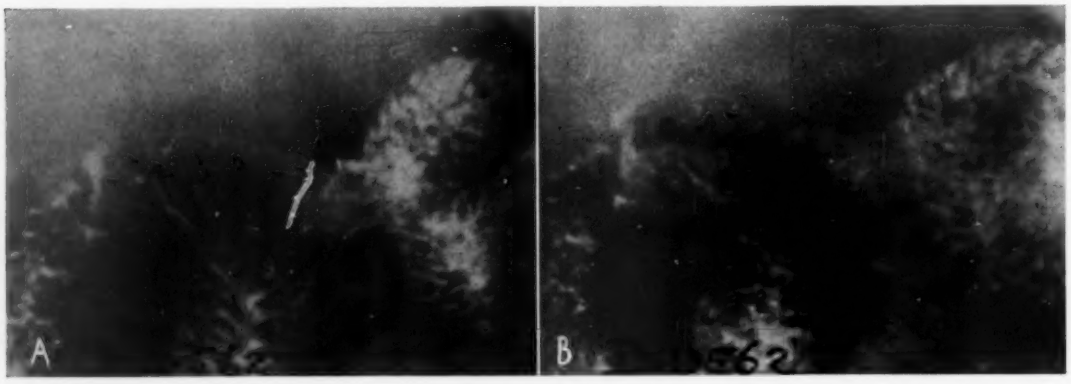

FIG. 1, *A* and *B*. Case 1. Normal cap and duodenum. Double contrast delineation of cap, which is distended with air. The base of the cap is overlapped by the terminal duodenum.

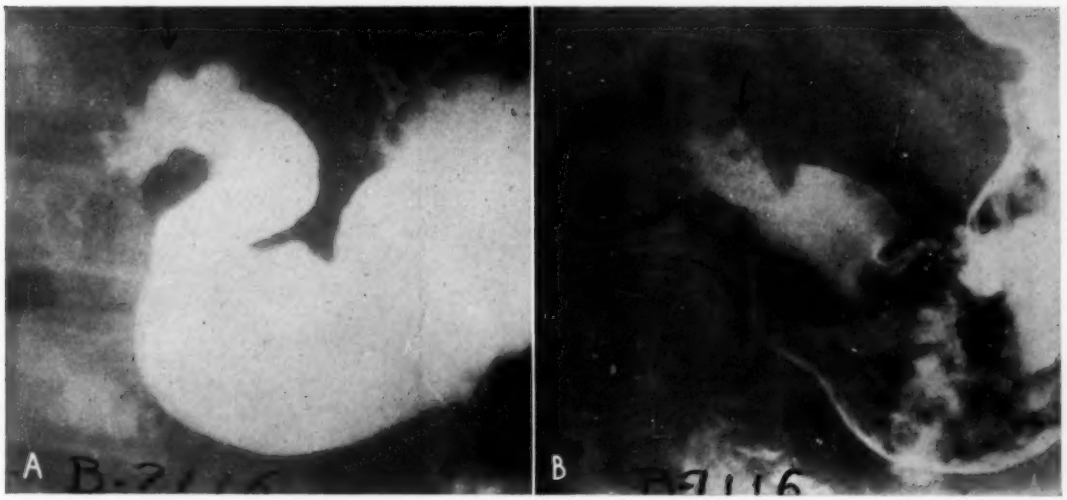

Fig. 2. Case II. History of repeated gastrointestinal hemorrhages for fifteen years, the last one about eight months ago. Previous diagnosis of ulcer from cap deformity. The present oblique prone roentgenogram, *A*, shows the deformity of the cap and also quite definite evidence of a crater. The crater is definitely visualized on the superior border on the oblique supine view, *B*.

in the hands of those expert in the palpatory maneuver.

Since 1929, following the work of Berg, Chaoul, Forssell, Åkerlund, and others, the use of compression technique, in roentgenography of the stomach and duodenum, with only slight or moderate filling with an opaque medium, has been emphasized for study of the mucosal pattern and demonstration of pathological conditions otherwise hidden. This has added greatly to our success in demonstrating some lesions roentgenographically, which could otherwise be shown only by palpation under the roentgenoscope.

In 1935, Hampton[1] called attention to the possibility of demonstrating, in the

[1] Hampton, A. O. Roentgen demonstration of bleeding duodenal ulcers. Read before the American Roentgen Ray Society, Atlantic City, September, 1935.

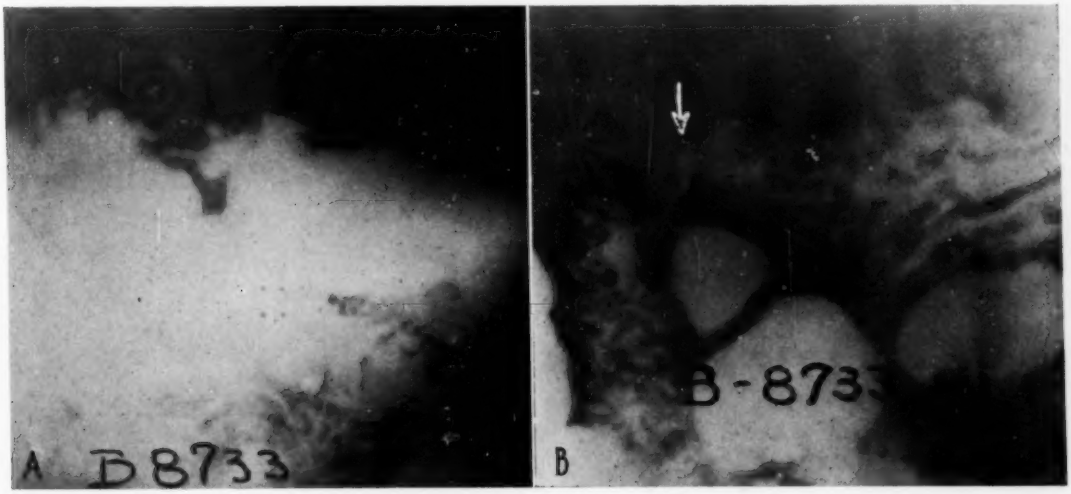

Fig. 3. Case III. Pain in epigastric region. Two weeks ago passed a large amount of blood by rectum. Ulcer of superior border of cap, best shown on oblique prone view, *A*. This is also shown in the oblique recumbent position, *B*. Three large duodenal diverticula.

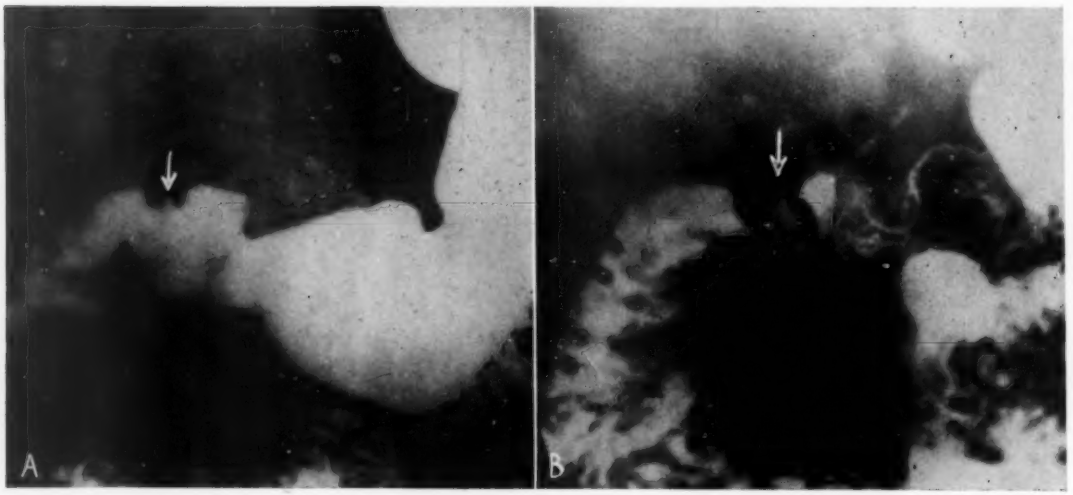

FIG. 4. Case IV. *A*. Duodenal ulcer as shown in the oblique prone position; *B*, the same ulcer shown in the oblique recumbent or supine position.

recumbent and left oblique recumbent positions on the roentenoscopic table, without the use of any dangerous palpatory procedure, the presence of ulcers on the posterior wall of the cap in cases of bleeding presumed to be from a duodenal ulcer. Frequently, as is well known, these cases are not amenable to definite direct proof, especially those cases where no characteristic ulcer symptoms have been present. This has been thought to be due to the early occurrence of bleeding from a recent ulcer, an ulcer of insufficient duration to have caused enough irritation to produce any characteristic deformity. This consideration and the inadvisability, and even danger, of the usual palpatory roentgenoscopic examination, in addition to the frequent shallowness of the crater, have made the positive diagnosis of duodenal ulcer difficult in certain cases of sudden hemorrhage. I have found the procedure of Hampton useful both in roentgenoscopy and roentgenography, using for the latter the roentgenoscopic tube, with the cassette anterior to the patient.

FIG. 5. Case V. *A*. Ulcer on superior border shown on the usual serial films; *B*, film made in the oblique supine position shows two craters.

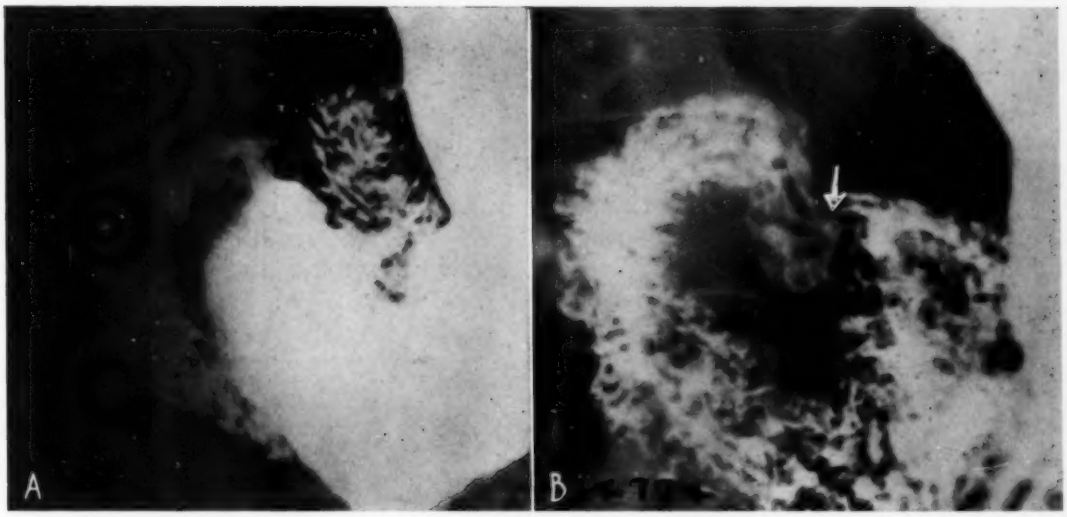

Fig. 6. Case vi. Severe pain in left scapular region for ten days without cough, chill or fever. Chest negative clinically and roentgenologically. Diagnosis appeared to be myositis. Marked deformity of cap in the oblique prone, deformity and probable crater in the prone position, *A*. Definite crater in the oblique supine position, *B*. Symptoms responded promptly to ulcer treatment.

In the past few months I have frequently used this procedure instead of compression in cases of suspected or definite duodenal cap ulcer without bleeding, and especially in cases of suspected ulcer at the junction of the cap and second portion of the duodenum, i.e., beyond the more usual site of duodenal ulcer. Ulcer at this point is, in my experience, not rare. Evidence of it is usually readily demonstrable roentgenoscopically, and, especially on serial films made in the right lateral horizontal position. Frequently, however, there is some uncertainty as to the actual pres-

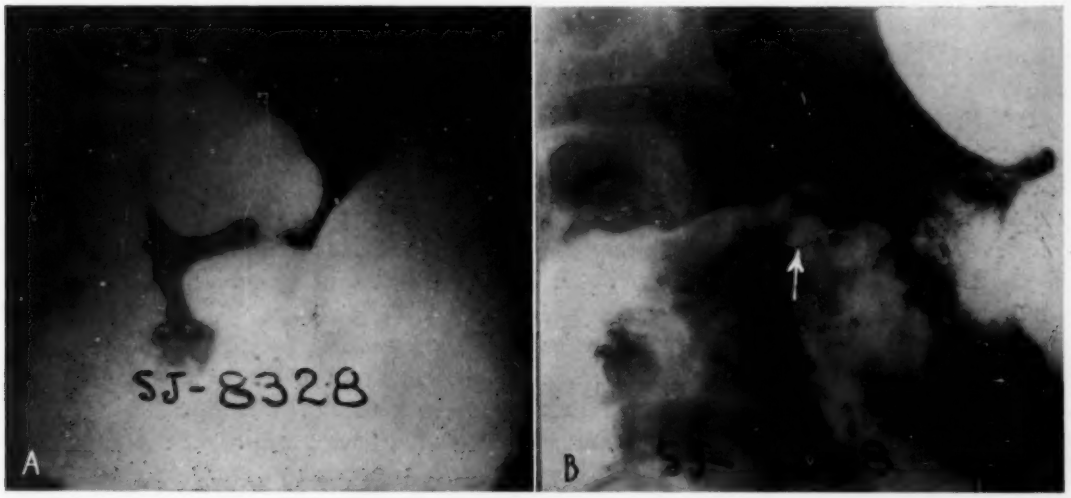

Fig. 7. Case vii. Pain and tenderness in upper abdomen for past three months, with some vomiting. Although there had been a previous roentgen diagnosis of duodenal ulcer in 1930, with several remissions and recurrences since, the present condition was thought to be acute cholecystitis until an active ulcer was demonstrated. The oblique prone position showed an apparently normal cap, *A*. Prone position showed a definite deformity and crater. Confirmed in the oblique supine position, *B*. The extreme base of the cap is partly obscured by barium in the duodenojejunal junction.

ence of an active ulcer, either in the cap or distal to the cap. In these cases I have found roentgenoscopy under the screen, with the patient lying on the table in positions varying from the recumbent to rotation to the left up to 45 degrees or more, of considerable value at times in demonstrating the presence or absence of a crater. The position with reference to the posture of the patient may be described as made without compression. An ulcer crater, at least on the posterior wall of the cap, is then shown by the fleck or pool of barium of varying density and size, depending on the size, depth and location of the crater. This persists during observation and palpation. Mucosal folds characteristically radiating from the crater are found in some cases. Ulcer on the posterior wall will, of course, be shown most

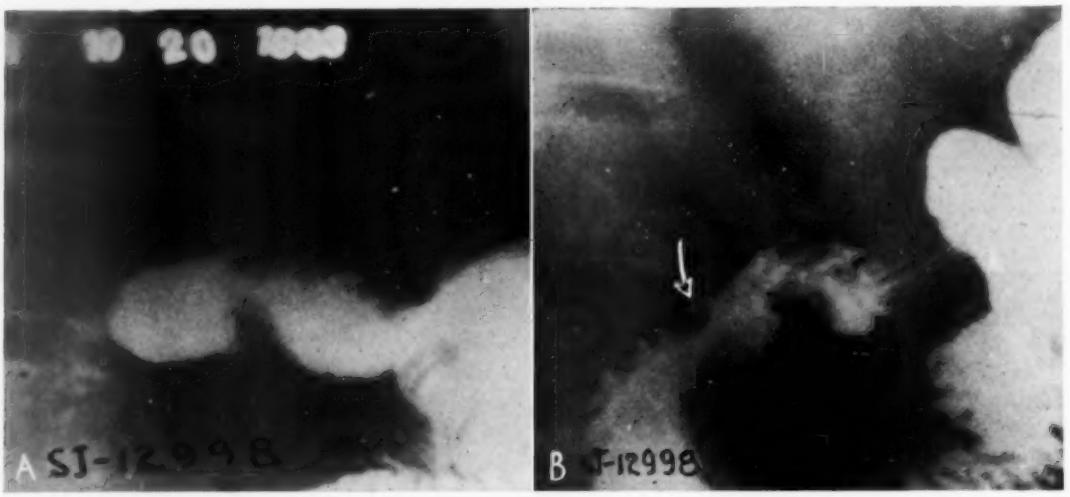

FIG 8. Case VIII. Upper abdominal pain. Duodenal cap remains almost constantly well filled and presents a normal appearance on the oblique prone position, *A*. There is a constant constriction just beyond the cap. A definite ulcer was best demonstrated in the oblique recumbent position, *B*.

the left oblique supine or recumbent position. When films are made, the position with reference to the roentgenographic exposure with the roentgenoscopic tube, would be left posterior—right anterior oblique. The roentgenoscopic description may be the same as the roentgenographic, or may be designated as the first oblique diameter. It is perhaps simpler and less confusing to designate the position as the right anterior oblique horizontal, as this describes the relation of the screen and cassette to the patient.

The actual crater is, by this method, sometimes brought out as definitely on films made on the roentgenoscope, as on films made under compression of the cap in the erect position, and frequently more definitely than on the usual serial films clearly. It is as yet uncertain whether the method has any great reliability for ulcers on the anterior wall. Ulcers on the borders of the cap can usually be shown. One must, of course, guard against interpreting a pool of barium caught in a mucosal fold or pocket as an ulcer. This, however, is no more difficult than with compression and is usually fairly easily done.

As a rule, the method is applied as an accessory to the routine examination. The patient is first examined in the usual manner, in the erect posture, if able to stand. If this is not advisable, the erect examination is omitted. The erect examination is followed by the routine examination of the cardiac portion of the stomach in the recumbent, oblique and left lateral recumbent positions. The patient then turns in

the same direction and the stomach and duodenum are successively observed in the prone, oblique and right lateral positions. When the stomach is emptying freely and the duodenum is well filled, the patient continues to turn in the same direction until again in the supine or recumbent position, having completed a full revolution, and now as much farther toward the left as will best bring the entire duodenum, but especially the cap and upper second portion, into the most extended position. The object is to obtain a position and a rate of emptying such that the mucosa of this region can be effectively studied. The cap and upper second portion of the duodenum are in most cases accessible to palpation in this position, at least during inspiration, and if the case is not one of too recent bleeding, or suspected impending or partial perforation, the cap and upper duodenum are now carefully palpated, as well as passively observed for evidences of abnormality in function, character of the mucosal folds, and evidences of deformity or an ulcer crater. Immediately following the screen observations several roentgenographic exposures should be made with the roentgenoscopic tube and with a small diaphragm opening, with the patient in the same oblique recumbent position, for record and later comparison, or to determine more definitely a questionable roentgenoscopic finding. These roentgenograms may be made singly, or preferably with the aid of a simple apparatus permitting four serial exposures on an 8″×10″ or 10″×12″ film. It is advisable to make films with the roentgenoscopic tube in order to get the cassette as close to the pyloric end of the stomach and duodenum as possible. These films should not be made with the tube above the patient.

The accompanying illustrations will serve to indicate the findings obtained.

SUMMARY AND CONCLUSIONS

Attention is called to the possibility of demonstrating certain ulcers of the duodenum roentgenoscopically and roentgenographically in the right anterior oblique horizontal position. The method is of value in demonstrating the ulcer crater in certain cases where no definite or characteristic deformity exists and where there is doubt as to activity in the presence of a characteristic ulcer deformity. It is also valuable where the patient for any reason cannot be examined in the erect position, as in cases of bleeding and suspected impending perforation, where palpation and compression may not be used. From present experience, it is of definite value only if the ulcer is on the posterior wall or on the borders. Care must be exercised not to mistake barium caught in a mucosal fold for an ulcer crater. The method is simple and can easily be carried out routinely as an adjunct to the usual examination. The position must be so chosen as to yield the most satisfactory lengthening out of the upper duodenum and the proper rate of emptying to maintain a small amount of barium in the cap and duodenum. It should be done at the first examination, if possible, or at least before opaque filling of the splenic flexure and descending colon have taken place, in order to avoid confusion.

A ROENTGENOLOGIST LOOKS AT SINUS DISEASE*

By KARL KORNBLUM, M.D.
PHILADELPHIA, PENNSYLVANIA

DISEASE of the paranasal sinuses constitutes an extremely difficult problem whether considered from the point of view of the rhinologist, the roentgenologist or the patient. Sinusitis is so prevalent that the entire population, in this part of the country at least, may readily be divided into two groups, namely those individuals having sinus disease with symptoms and those having sinus disease without symptoms.

Most radiologists will readily admit that in the entire field of roentgenology nothing affords them greater difficulty than examination of the paranasal sinuses. For this reason, I daresay, the poorest and most unsatisfactory results of most roentgenologists is in the domain of sinus roentgenography. These are the films for which he is most frequently called upon to offer apologies and this in spite of the fact that much has been written in regard to the roentgen technique in examination of the sinuses. In considering the problem of the paranasal sinuses, there appears to be some fundamental facts that either are not generally known or have been given too little consideration. An analysis of the various factors that play a rôle in the examination of the sinuses and in the interpretation of the resultant roentgenograms should aid both the rhinologist and roentgenologist to a better understanding of this diagnostic procedure and may lead to a practical solution of the problems presented by sinus roentgenography. This is primarily the purpose of this contribution.

Early in my career as a roentgenologist, I became impressed with the frequency of requests for sinus examinations and also with the prevalence of sinus disease, as revealed by the roentgen ray. Negative sinuses were so uncommon that one had reason to marvel when such were encountered. It seemed incredible that so many individuals could have sinus disease and I began to question the accuracy and the value of the roentgen examination. This skepticism naturally made me want to know the benefits derived by the clinician from a roentgen examination of the sinuses. I pondered these facts for a number of years, talking the matter over with both roentgenologists and rhinologists, and I finally concluded that the clinical examination of the sinuses is probably as difficult of interpretation as is the roentgen examination, often being rather inconclusive. It seemed, therefore, that any procedure which might promise aid in disclosing disease of the sinuses would naturally be welcomed by the clinician. I have reason to believe, however, that this conclusion is erroneous; that most rhinologists are rather confident of the results of their sinus examination. The reason, then, for the roentgen examination of the sinuses would appear to be that it serves to confirm the clinical diagnosis; it may aid in detecting factors responsible for the failure of sinus disease to respond to treatment; it occasionally reveals significant disease in the presence of a negative clinical examination and finally it is of much value in depicting the anatomy of sinuses requiring operation.

There seems to be some difference of opinion among rhinologists as to the value of the roentgen examination in sinus disease, if one may judge by the variable extent to which this diagnostic procedure is utilized. This disregard of the roentgen examination by some clinicians is due to the frequency with which the clinical and roentgen findings are at variance. The rhinologist, being more familiar with the clinical aspects of sinus disease, naturally

* From the Department of Radiology, Graduate Hospital, University of Pennsylvania, Philadelphia. Read before the Philadelphia Laryngological Society, April 7, 1936.

places more reliance in his clinical findings than in those of the roentgen examination. With the roentgenologist, the process is just the reverse. His training is such as to make him believe that the roentgen ray is almost infallible; therefore, when the clinical results do not conform with the revelations on the roentgenogram, he is likely to assume that the clinician has been in error again. There is much to be said on both sides of this question. Unless an attempt is made to correlate the two methods of examination, one cannot hope to arrive at the true state of affairs, and the patient is deprived of the full benefits of a diagnostic procedure to which he is justly entitled and which he most earnestly needs as far as an understanding of diseases of the paranasal sinuses is concerned.

I know of no roentgen examination in which the personal equation plays such an important rôle. Some years ago, I conducted a minor bit of investigation that convinced me of the importance of the personal element in the interpretation of sinus roentgenograms. As a beginner in roentgenology at the University Hospital, I was somewhat concerned with the difficulty I was having in the interpretation of sinus films. In order to check my own interpretations, I made it a practice to show sinus roentgenograms first to Dr. E. P. Pendergrass and then to Dr. H. K. Pancoast, my mentors in radiology, getting their opinions independent of each other. I did this for some time and was surprised to find how seldom the three of us were in complete agreement. In almost every instance, there was some difference of opinion and this in spite of the fact that both Dr. Pendergrass and I had been trained by Dr. Pancoast. If such variable results prevail among workers in the same department, where all factors except the personal element are the same, how much greater must be the variation in interpretation among roentgenologists of unlike training, working under different conditions and using different techniques. Furthermore, I have on numerous occasions checked my own interpretations by reading the same films some weeks later and have frequently found that the second interpretation has not been in agreement with the original report. Now obviously there is something wrong somewhere. Such variations in interpretative results do not occur in other types of roentgenographic work. Unfortunately, the opportunity is not often afforded to check the results of sinus interpretations, since only a small percentage of patients having a roentgen examination of the sinuses come to operation and few, if any, have autopsy verification. One can of course check with the results of the clinical examination but one can never be absolutely certain as to the accuracy of the findings of such an examination. Especially is uncertainty likely to exist when the results of these two methods of examinaton do not harmonize.

In regard to checking with the clinical examination, there occurs a pitfall which the roentgenologist unconsciously encounters. After a few years' association with a given group of rhinologists, he soon comes to know their individual peculiarities and professional tendencies. Therefore, his reports to them on sinus examinations are likely to be influenced by his knowledge as to whether they maintain radical or conservative views regarding diseases of the paranasal sinuses. That such an extraneous factor can influence roentgen interpretation is due to the fact that in sinus roentgenography the personal element plays such an important rôle. This does not occur in other forms of roentgenography, such as of the chest and gastrointestinal tract. Roentgen interpretation should be, above all else, objective and should be totally divorced from any extraneous influences and preconceived ideas.

When I say that the roentgen examination should be divorced from extraneous influences, I do not mean to exclude the aid that may be derived from a knowledge of the clinical aspects of the case. On the contrary, I am convinced that one cannot use the roentgen examination intelligently

without careful correlation of the clinical and roentgenologic findings. The roentgenologist must not, however, permit himself to be unduly influenced by the clinical manifestations. To avoid this error he should acquire the habit of first carefully examining the roentgenograms and forming an opinion as to what they show before consulting the history of the case. Then by a correlation of the clinical and roentgenological data, he is ready to arrive at his final conclusion. Again I would emphasize the importance of keeping the roentgen examination as objective as possible.

And this brings me to a very important phase of the roentgen examinations of the sinuses. For an intelligent interpretation, one must have at hand the essential clinical facts in the case. This should be supplied by the clinician along with the request for the examination and should consist of a brief statement as to the patient's chief symptoms, the duration of the condition, the positive clinical and laboratory findings and, most essential, data concerning any operative procedures upon the nose or sinuses. This information should be brief. The roentgenologist's use of these data often leads to the accusation that he is rendering a clinical rather than a roentgen diagnosis. One must not lose sight of the fact that there is no such thing as a roentgenological, a neurological, an orthopedic or laboratory diagnosis. There is but one diagnosis and that is a clinical diagnosis. The roentgenologist uses the roentgen ray in arriving at a clinical diagnosis in the same manner as the neurologist uses his specialized knowledge of neurology in arriving at his clinical diagnosis. The roentgenogram is to the roentgenologist what the physical examination is to the clinician; in other words, the roentgenogram is the roentgenologist's physical examination. Since the clinician cannot interpret the results of his physical examination without some knowledge of the patient's history, so it is with the roentgenologist, he cannot render an intelligent interpretation of the roentgenograms without knowing the history of the case.

At a recent meeting of the Philadelphia Roentgen Ray Society, Dr. Frederick M. Law of New York City, during one of his excellent discourses on the paranasal sinuses, expressed grave fear that the rhinologists were becoming too proficient in the interpretation of sinus roentgenograms. I am sure that Dr. Law expressed himself in this manner, not so much because he felt his statement to be actually true, but more because of his desire to stimulate the roentgenologists to greater effort. It is true that the clinician in every specialty is taking a greater interest in roentgenology and is able to look at roentgenograms more intelligently than the physician of ten or fifteen years ago. This is as it should be. When the roentgen ray has lost its mysticism and when the roentgenogram is no longer a conglomeration of unintelligible shadows, then it will have come into its own as one of the greatest of modern medical appliances. There is no reason why the clinician should blindly accept the report of the roentgenologist. There is no reason why he should not equip himself to interpret roentgenograms to the best of his ability. The qualified roentgenologist has nothing to fear from this apparent invasion of his specialty. The competent laryngologist is not concerned because some general surgeons persist in removing tonsils. He knows full well the ultimate results of such practice. The obstetrician is not concerned because the family physician insists upon doing midwifery, and the urologist is confident that he is more competent to perform a nephrectomy than the general surgeon or gynecologist. The old adage, "A jack-of-all-trades and a master of none" is just as true in medicine as in any other walk of life. A specialist who doesn't know his limitations usually doesn't know much of anything else. The rhinologist who feels that he does not need the help of a competent roentgenologist in the interpretation of sinus roentgenograms will not

usually attain much eminence in his chosen specialty. But I wish to lay stress on the use of the term "competent roentgenologist" because I am cognizant of the fact that clinicians have been virtually forced into the interpretation of roentgenograms due to the incompetency of many roentgenologists. I am convinced that the rhinologist would be only too glad to consult the roentgenologist, if he could feel confident of receiving intelligent help. The growth of roentgenology has been so rapid that the supply of competent roentgenologists has been inadequate to meet the demand. The recent creation of the American Board of Radiology, will, it is hoped, soon correct this condition. Unless one is willing to give the time and energy to master the fundamentals of roentgenology, he cannot hope to become qualified for roentgenological interpretation. When Dr. Law set to work to equip himself to interpret roentgenograms of the paranasal sinuses and mastoids, he had to give up the practice of otolaryngology. There are many factors which enter into the interpretation of roentgenograms of which the clinician can have no conception. This is particularly true of the paranasal sinuses, and I wish briefly to direct attention to some of the factors which commonly lead one astray in the interpretation of sinus roentgenograms.

From a technical point of view, the paranasal sinuses afford one of the most difficult of all roentgenologic examinations. This procedure calls for a technical feat which, with the exception of the mastoids, is not required in any other type of examination. An attempt is made to obtain, at one and the same time, visualization of the soft tissues as well as of the bony structures of the sinuses. In other parts of the body one does not consider undertaking such a difficult task. Soft tissue technique differs radically from the requirements for bone visualization. In the chest, there is a vast difference in the technique employed when one desires information of the heart and lungs in contrast to the bony thorax. It is this unusual requirement in sinus roentgenography that calls for as nearly perfect technique as can be obtained. It is for this reason that one so frequently encounters under- and overexposed sinus films. Slight variations in exposure result in tremendous changes on the roentgenogram. An underexposed film fails to give satisfactory information regarding the bony structures and often tends to exaggerate the shadows of the soft parts. Overexposure, on the other hand, blots out the soft tissue detail. It is for this reason that the Potter-Bucky diaphragm is not often employed in sinus work. These are the factors which the clinician cannot fully appreciate and his training does not enable him to compensate for variations in roentgen exposures.

Positioning of the head is another factor of vital importance. It is often difficult to appreciate how a slight change in the position of the head can result in such a vastly different effect on the roentgenogram. The same distortion may be produced by incorrect angling of the roentgen tube. In the technique most commonly employed, a cone is utilized so that nothing but the region of the paranasal sinuses is included on the resultant roentgenogram. Correct centering of the tube therefore becomes a matter of the utmost importance.

Another factor which greatly influences the end-result in sinus roentgenography is the great variation to be found in the anatomical make-up of the head. There is considerable variation in size and shape in different individuals. This is usually taken account of by actually measuring the head and thus the exposure factors are somewhat satisfactorily controlled, but the variation to be found in the thickness of the bones of the skull and in their density are factors which cannot be predetermined and which markedly influence the type of exposure obtained. These technical details cannot be fully appreciated by anyone who has not actually engaged in roentgenographic technique and yet from an interpretative point of view errors in technique may render an examination utterly worthless.

These technical difficulties have led to a great deal of variation in the technique employed by different roentgenologists. Numerous positions and technical modifications have been devised and yet none seems to give universal satisfaction. Several years ago, I attended a meeting of the Philadelphia Laryngological Society and heard a paper presented on sinus disease. I was greatly amused when one of the clinicians, during the discussion, expressed great indignation over the fact that in none of the three hospitals with which he was connected did the sinus films present the same appearance. As he stated, "How in the world was he to interpret films under such variable conditions." His remarks made it quite obvious that he was not well informed in regard to sinus roentgenography. The clinician must not lose sight of the fact that roentgenograms are made primarily for the roentgenologist to interpret and that the roentgenologist, therefore, employs the technique best suited to his purpose. Absolute standardization is not likely to be attained, any more than absolute standardization in surgical technique will ever prevail. Every surgeon uses that technique which insures him best results, regardless of the practice of his surgical colleagues, and the same is true of the roentgenologist.

As a matter of curiosity, I recently visited ten laboratories of private and hospital roentgenologists and in only two instances was the same sinus technique being employed. It was really surprising the great variation found in technique. The number of views made of the sinuses ranged from two to six. In the majority of instances, four exposures were made. The Caldwell position for the frontals and ethmoids and the Waters position for the maxillary sinuses were most generally employed. The greatest variation was found in the position used for the sphenoid sinuses. In most instances, the examination included a lateral view but there was no uniformity of purpose in the employment of this position. Stereoscopic examinations were rather exceptional. In no instance was the Potter-Bucky diaphragm utilized. Only a few roentgenologists were making sinus films in the erect position. In several cases a more elaborate examination was employed in private, as compared to the ward and dispensary patients. In general, the technical results found in the various laboratories were quite satisfactory as judged by present day standards. I do not believe there is another roentgen examination in which one will find a greater variation in technique. This merely emphasizes the fact already referred to that the paranasal sinus examination is a most difficult one and apparently not very satisfactory from the roentgenologist's point of view.

In this recent survey, I was also interested in the type of report given by the various roentgenologists. For the most part, these were rather short and confined to a mere statement as to the relative density of the various sinuses. In some instances, the roentgenological findings were interpreted in terms of pathology. Only rarely was much attention given to the anatomy of the sinuses. It has always been a problem to know just what and how much to report in a sinus examination. If one is to describe in detail the various anatomical and pathological changes found in the sinuses the report would be of interminable length and extremely boresome. The busy clinician would not take time to read such lengthy reports. It has seemed to me that, as a rule, when a sinus is negative nothing more need be said about it. From a practical point of view, we are interested only in those sinuses which are diseased, so it seems useless to give a lengthy description of the anatomical variations of negative sinuses. In diseased sinuses, however, one should describe the anatomical variations and the condition of the bony walls. Unfortunately, in many instances the pathological changes obscure the anatomical and structural details.

There are some physicians who believe that the function of the roentgenologist should be confined to a mere description

of the shadows seen on the roentgenogram without an attempt to interpret such shadows in terms of pathology. Roentgenology would lose much of its value and fascination if such a method were pursued. The remarkable success that has attended roentgenological investigation of various organs of the body in which definite disease entities are demonstrated, such as pulmonary and osseous tuberculosis, peptic ulcer and various types of bone tumors, bears witness to the fact that on the roentgenogram specific diseases may produce characteristic and in many instances pathognomonic changes. It is now possible in some cases to recognize the histological structure of brain tumors by the changes found on the roentgenogram. While I am willing to admit that in the paranasal sinuses it is much more difficult to recognize the precise pathological changes that have occurred, nevertheless one should endeavor to give a pathological interpretation. An attempt should be made to recognize the changes as either acute or chronic; a statement should be made as to whether the opacity is due to hyperplastic tissue or the presence of an exudate, with or without evidence of a fluid level, and whether the disease is confined to the mucous membrane or also involves the bone. The presence of an osteomyelitis should be looked for and polypoid formation of the mucous membrane should be reported. One should constantly keep in mind the possibility of neoplasms. Attention should be given to the intranasal structures and abnormal changes in the nasal septum and turbinates should be reported. Since there are few sinuses that are absolutely normal the roentgenologist may, if he considers it advisable, express an opinion as to whether or not he regards the changes present as of clinical significance. Roentgenologists of experience may become very accurate in their opinion in regard to the clinical significance of the roentgenological changes in the sinuses and other parts of the body. However, it is not primarily the function of the roentgenologist to pass upon the clinical significance of the roentgenological findings. Such findings can be properly evaluated only by a correlation with the history, physical examination and other laboratory and diagnostic data. This final correlation must be done by the clinician. This should not, however, deter the roentgenologist from expressing an opinion which may be accepted or rejected by the clinician as his analysis of the case dictates. As regards the paranasal sinuses, the roentgenologist cannot be too dogmatic in his opinion and must be prepared to find himself frequently in error. This is no indictment of his ability but merely emphasizes the fact that, as regards the paranasal sinuses, the roentgen examination leaves much to be desired.

The roentgenologist is frequently criticized for the fact that according to his reports nearly everyone has sinus disease. Pathologically this is practically the truth. It must not be forgotten that the roentgen ray reveals pathological changes both past and present. In this repect, it resembles the microscope. Take the case of the appendix as an example. The pathologist can find evidence of disease either acute or chronic in every appendix that he examines, yet this does not mean that the original owner of such an appendix necessarily suffered from appendicitis. The same may be said of the gallbladder. As a matter of fact, most of the organs of the body are capable of rendering function compatible with good health in the presence of definite disease. It does not follow, therefore, that a patient is suffering from sinusitis simply because the roentgen examination reveals pathological changes. The roentgenologist must report what is revealed to him by the roentgenogram; the changes found become significant only when correlated with the rest of the clinical picture.

The fact that the roentgen examination reveals evidence of disease that may not be of clinical significance is often the source of much confusion. I can appreciate the quandary of the rhinologist who reports to

a referring physician that his clinical examination of the sinuses is negative and then have the roentgenologist report extensive sinus disease. This is a very frequent occurrence. It is difficult for the average physician to understand such a discrepancy and he is often at a loss to know what to do. In such cases, the rhinologist and roentgenologist should consult with each other and an effort should be made to bring the two methods of examination into harmony. The medical profession needs to be educated to the fact that the roentgen examination in many instances reveals evidence of previous disease as well as present pathology and that not all the changes present are clinically important. One of the best examples of this kind is the frequency with which old healed tuberculous lesions are found in the lungs. In a clinical survey of the chest such findings in many instances must be entirely ignored. They must be recognized as scars and nothing more. The same is true of the sinuses. Seldom will the roentgen examination stand alone, seldom will it yield a diagnosis in its own right. It is only the intelligent correlation of the roentgenological with the clinical manifestations that gives to the roentgen ray its great diagnostic value.

There are other reasons for the discrepancies which sometimes exist between the clinical and roentgenological examinations. One must not lose sight of the fact that the mucous membrane of the upper respiratory tract is subject to rather marked and rapid changes, showing considerable variation from time to time in its degree of congestion. The state of the mucous membrane will be indicated by the character of the shadow produced on the roentgenogram. While the clinician, by direct inspection, may recognize the true condition of the mucous membrane, on the roentgenogram a simple congestion may simulate a more serious condition. It is for this reason that the same sinuses may vary in appearance when examined at different times. For instance, there is considerable difference in the appearance of the ethmoids, depending on whether or not the turbinates are producing nasal obstruction as the result of congestion. For a proper comparison, the clinical and roentgenological examinations should be made under identical conditions as far as this is possible. One might adopt the plan advocated by Dr. S. R. Skillern* in having the roentgen examination done immediately before his second clinical examination. Thus conditions are the same at the time of both examinations and comparison of the two methods is more reliable. It should be remembered that intranasal manipulations just prior to a roentgen examination may produce temporary changes; thus the effect of shrinking the turbinates and slight traumatisms producing hemorrhage or clots may be depicted on the roentgenogram. We have occasionally seen a fluid level after irrigation of the maxillary sinuses. Without knowledge of such an irrigation, one cannot properly interpret such a fluid level. Previous operations upon the sinuses produce marked changes in their appearance. This is especially true of the ethmoids which appear very dense and clouded after an ethmoidectomy. Knowledge of these facts enter into the proper interpretation of sinus roentgenograms.

The roentgenologist occupies a rather unusual position in the medical profession. His daily work brings him in contact with practically all of the medical specialties and he must possess a broad general knowledge of medicine. His position affords him an opportunity to impartially observe the modern trend of medical practice and he soon learns to judge the value of various diagnostic and therapeutic procedures. Because of this position, he is frequently consulted by his medical colleagues in matters pertaining to therapy. I consider it beyond the province of the roentgenologist to indicate therapeutic measures in his roentgen report beyond that pertaining to radiation therapy, no matter how competent he may be in matters of general therapeutics.

* Personal communication to the author.

However, where his advice in regard to therapy is specifically requested, I see no reason why the result of his experience should not be placed at the disposal of the clinician. The roentgenologist is frequently consulted in regard to therapy in sinus disease by those having no special knowledge of the paranasal sinuses. I am inclined to believe that roentgenologists, for the most part, are rather conservative and pessimistic as regards treatment in sinus disease, especially where surgery is involved. They are probably not entirely justified in their position in this matter but certainly the daily experience of the roentgenologist is such as to make him ultraconservative. The frequency with which patients who have had multiple operations on the sinuses are referred to him for examination is sufficient to impress him with the futility of surgery in many instances. I recognize that this is a distorted point of view, since patients, who have been successfully operated on, do not subsequently return to the roentgenologist. He sees only those patients in whom there has been a persistence of symptoms, but certainly these are in sufficient numbers to make a profound impression on any roentgenologist associated with an active hospital service.

The paranasal sinuses are frequently investigated in the search for foci of infection and as the etiological factor in hay fever and asthma. I have been impressed with the infrequency with which roentgen evidence of sinus disease is found in such cases. Most of the negative sinuses that I see are in patients in whom a search is being made for some focus of infection. One exception to this, however, is in patients with eye disturbances in whom disease of the sinuses is frequently found. Also in bronchiectasis there appears to be a definite relationship to sinus disease. The high incidence of sinus disease in the general population, however, makes it difficult to evaluate its relationship to bronchiectasis. Statistics in this regard are open to considerable skepticism. The frequency with which severe chronic sinus disease is unassociated with bronchiectasis and the not at all uncommon finding of bronchiectasis without sinus disease makes it evident that factors other than the sinuses are frequently responsible for this condition.

A consideration of bronchiectasis brings one in contact with sinus disease in children. The difficulties already discussed in regard to the roentgen examination of the sinuses in adults are greatly enhanced in children. Lack of cooperation makes it extremely difficult to secure satisfactory roentgenograms in infants and young children. The undeveloped and poorly developed sinuses and the small size of these cavities make roentgen interpretation a hopeless proposition in many instances.

I have attempted to present the problem of the paranasal sinuses as it has impressed itself upon me as a roentgenologist. By this time, it must be quite evident that I do not have a high regard for the present value of the roentgen examination of the sinuses. I am convinced, however, that this procedure can be made more valuable but do not believe that this can be accomplished until the rhinologist and the roentgenologist attack this problem together. I have already indicated in some detail the difficulties confronting the roentgenologist but would like to discuss briefly some of the obstacles to be encountered by the clinician in sinus roentgenography. The rhinologist quite naturally feels that his intimate knowledge of the anatomy and pathology of the paranasal sinuses and his knowledge of the history and clinical examination give him a distinct advantage in the interpretation of sinus roentgenograms. I am convinced that knowledge of the clinical aspects of a case often places one at a distinct disadvantage. The clinician examines the sinus roentgenograms with preconceived ideas formulated while taking the patient's history and during his clinical examination. Having made up his mind that the patient has an ethmoiditis, he needs only to look at the sinus films to confirm his diagnosis. There is no denying

the fact that "we see what we want to see," and the clinician often reads into the films conditions that do not exist. He is, in other words, rendering a subjective rather than an objective interpretation. As already indicated, the proper procedure for roentgenographic interpretation is to examine the roentgenograms carefully, interpret the films on the basis of what is seen, then inquire into the clinical aspects of the case and finally render an interpretation based upon a correlation of the clinical and roentgenological findings. Only in this way can errors be avoided.

I have already referred to the great influence played by technical factors in the end-results of sinus roentgenography. The rhinologist is at a distinct disadvantage in this regard, since he has not been trained to recognize technical errors and variations to be found in sinus roentgenograms. I frequently find the clinician attempting to interpret ethmoid sinuses in films not intended to show the ethmoids and he is frequently confused by the superimposition of the various structures of the head. Furthermore, sinus films frequently reveal evidence of disease not directly associated with the sinuses, such as deformations of the sella turcica, abnormalities in the orbits and hyperostoses commonly associated with brain tumors. The recognition of these conditions is of vital importance. These are but a few of the many difficulties to be encountered by the clinician.

This presentation has but a single purpose and that is to emphasize the absolute necessity of cooperation between the rhinologist and the roentgenologist. I am convinced that the full value of the roentgen examination can be obtained in no other way. This does not mean that the rhinologist and the roentgenologist need go into conference over every sinus roentgenogram. In many instances, the result of the examination is quite obvious. In the less obvious and more difficult cases, however, a consultation should be sought. Each should examine the films independent of the other and then all the facts, both clinical and roentgenological, should be freely discussed. I am convinced of the need of a more thorough and combined application of the efforts of the rhinologist and the roentgenologist to the problems of the paranasal sinuses. Each specialist should be afforded the benefit of the other's knowledge and experience.

I would suggest that in hospital practice one member from the rhinological staff and one from the radiological department be assigned to a study of the problems presented by the paranasal sinuses. These two individuals in consultation should study both clinically and roentgenologically each case having a roentgen examination of the sinuses. This team should have access to the operative findings so that these may be compared with the preoperative diagnosis. At least once each year a report should be made to the combined staffs of the rhinological and radiological services so that everyone may derive benefit from this intensive study. I am certain such a plan would be very fruitful and work to the benefit of all concerned, including the rhinologist, the roentgenologist and, above all, the patient.

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THE SALIVA CELL COUNT IN MYELOGENOUS LEUKEMIA*

By KENNETH D. A. ALLEN, M.D., *and* L. DICKEY, M.D.
DENVER, COLORADO

BECAUSE myelogenous leukemia is a fatal disease, medical readers often do not read articles of which it is the subject.

Recent literature has furnished certain data which, if practically applied to the therapeutic regimen of myelogenous leukemia, may increase the good results in some cases. Since Isaacs[10,11] demonstrated the behavior of the *saliva cell count* during and after irradiation, evidence is at hand which justifies a careful study of its use as a guide to therapy. Any procedure which will increase the length of a remission, raise the degree of the patient's efficiency during a remission or prolong useful life in myelogenous leukemia deserves consideration.

Another contribution to medical literature which stands out as greatly influencing the treatment of myelogenous leukemia is that of Stengel and Pancoast[22] in 1908.† This article suggested that the marrow regions of the long bones be subjected to irradiation as the major portion of the treatment, the spleen receiving only sufficient to control its size. The studies of these authors led them to believe that since the disease apparently originates in the marrow cavities, these are the logical areas to treat. Their method, of course, is still extensively used. The size of the spleen is often reduced materially during treatment of the bones only. An example of this is shown in Figure 12. Since the time of Stengel and Pancoast's presentation there has been little in the literature to materially affect treatment until Isaacs' contributions.

Isaacs furnished evidence that irradiation decreases the number of circulating leukocytes by stimulating their rapid maturation rather than by outright destruction. It is his opinion that myelocytes (and small lymphocytes) are accelerated in the completion of their life cycle and that they end their existence in the adult stage by dying or passing through the mucous membrane of the gastrointestinal tract primarily by leukopedesis. Isaacs and Danielian[12] had formerly demonstrated that the upper gastrointestinal and buccal mucous membrane is the route of excretion of the leukocytes in health, in disease and after irradiation. They acknowledge the contributions of Mauro,[13] Beckwith, Simonton and Williams, Bunting and Huston,[6] and others. Isaacs, in his report in 1930, further states that the primitive myeloblast and the myeloblast (Fig. 1) are influenced toward division (reproduction) instead of maturation. Thus, at times, irradiation of a patient whose blood contains myeloblasts not only fails to be of benefit but actually renders the blood stream less normal. It may permit the marrow to become packed with these abnormal cells and thereby secondarily obstruct erythrocytic production with resulting anemia, which impairs the patient's general condition. High marrow cell counts made since by Isaacs has confirmed this conception.‡

Isaacs also demonstrated that in health a fairly constant relationship exists between the cells in the saliva and those in the blood. Variation within the limits which he deemed normal seemed to be reciprocal. As the saliva count increases the blood count decreases, and vice versa. He reported also that in aleukemic leukemia, for example, as the leukocytes of the blood decrease in number the saliva count mounts. In several cases with leu-

† A bibliography of other pertinent articles is appended.

‡ Personal communication.

* From the Department of Roentgenology, Presbyterian Hospital, Denver, Colorado. We wish to acknowledge the generous technical assistance given by Dr. Paul Carson, Department of Clinical Pathology.

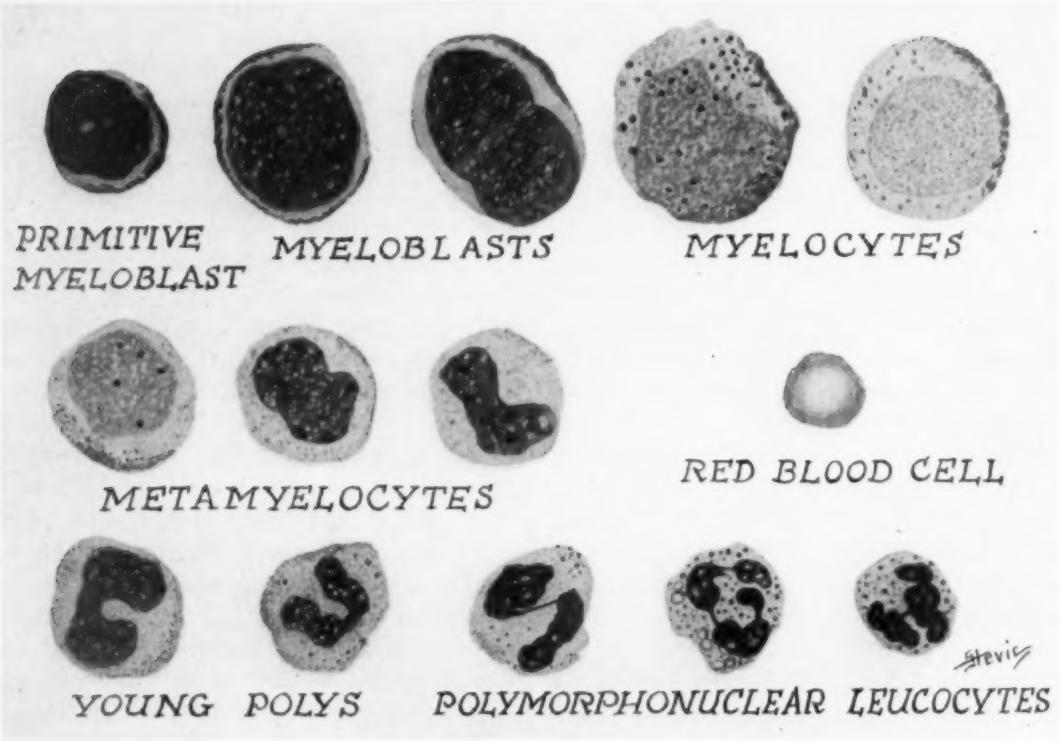


FIG. 1. Drawings of various types of blood cells present in blood smears of Cases I and III (see photomicrographs Figs. 6, 7 and 8).

kopenia which we have studied in recent months (not reported here) our findings have conformed to this conception. Isaacs further believes that an increase in saliva count, with a coincident decrease in the blood count under the influence of irradiation, indicates that the marrow cells are not yet exhausted. This very practical observation has made available a scientific guide for the determination of the amount and frequency of irradiation. The importance of a minute study of the red and white blood cells and routine saliva cell counts cannot be overemphasized.

This valuable contribution has aroused surprisingly little comment in the medical literature. It is therefore appropriate to record additional observations, the purposes of which are: (*a*) to subscribe to

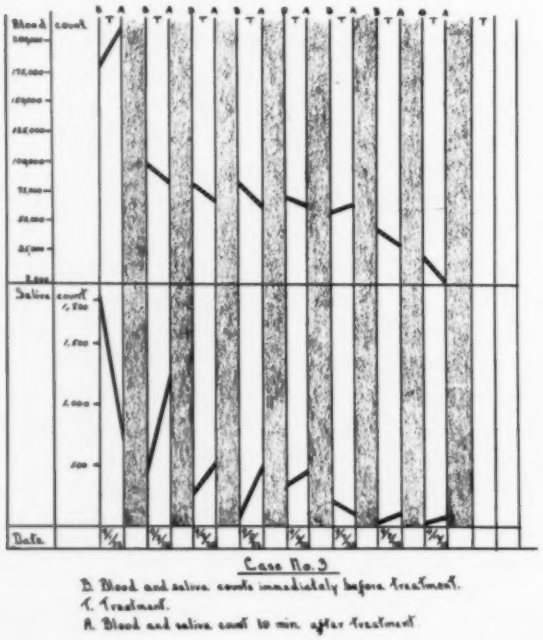


FIG. 2. Note the inverse relation between white blood cell count changes and saliva cell count changes resulting from irradiation. The descending blood count was also attended by a decreasing percentage of myelocytes, indicating a shift to the right (maturity). Note the initial rise of the white blood count (see also Figs. 3*a*, 3*b*, 4*a*, 4*b*, 5, 9, 10, 11, 13 and 14).

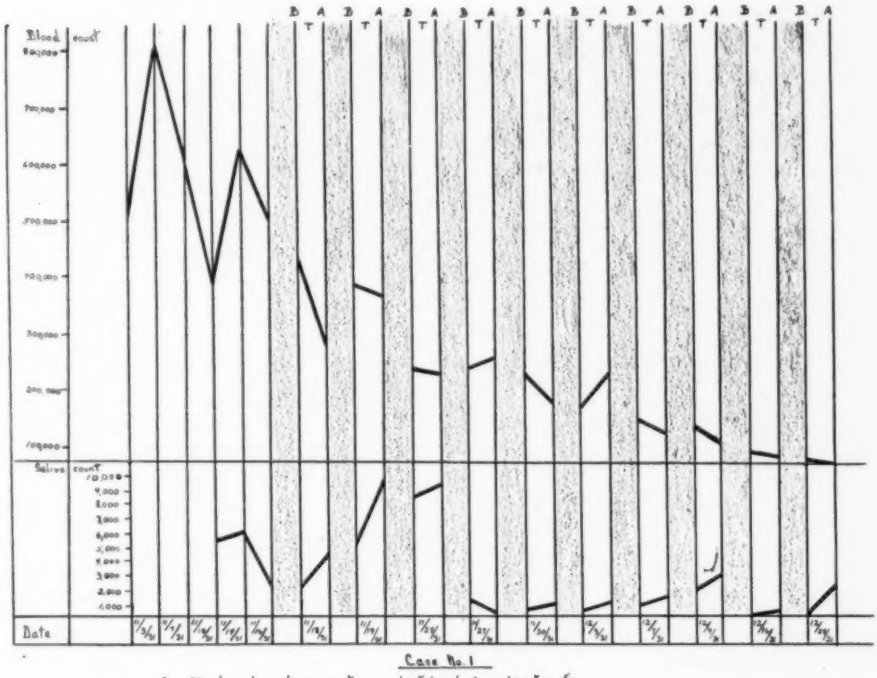


Fig. 3*a*. Blood and saliva white cell determination in relation to a first series of radiation therapy. Note the rise of white blood count to a maximum after the beginning of irradiation before the general downward trend was initiated and the general inverse relation of blood and saliva white cell curves.

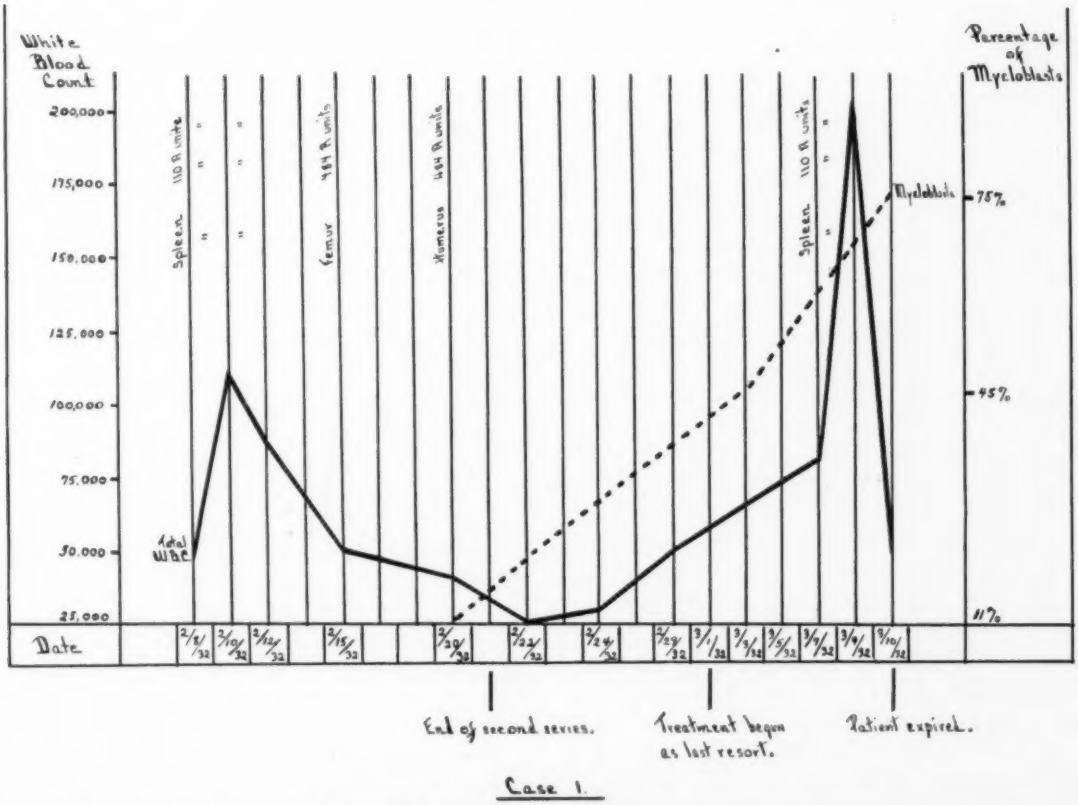


Fig. 3*b*. Note the detrimental effect of irradiation in the terminal stage when myeloblasts were predominating the blood picture. Myeloblasts began to appear shortly after the end of the second series of treatments and increased to 75 per cent a few days before death.

Isaacs' conception of the effects of irradiation on chronic myelogenous leukemia; (*b*) to urge frequent and detailed microscopic blood and saliva studies by those who treat myelogenous leukemia, not only during treatment but also during remissions and thereby add to the clinical evidence which determines the time for a subsequent series of treatments; (*c*) to proffer additional observations and relate them to therapy; (*d*) to summarize the value of saliva cell counts. This requires a brief description of 10 cases of chronic myelogenous leukemia and a more detailed consideration of their response to irradiation as depicted in graphs of blood and saliva counts. Many negative and positive points of lesser significance have been excluded.

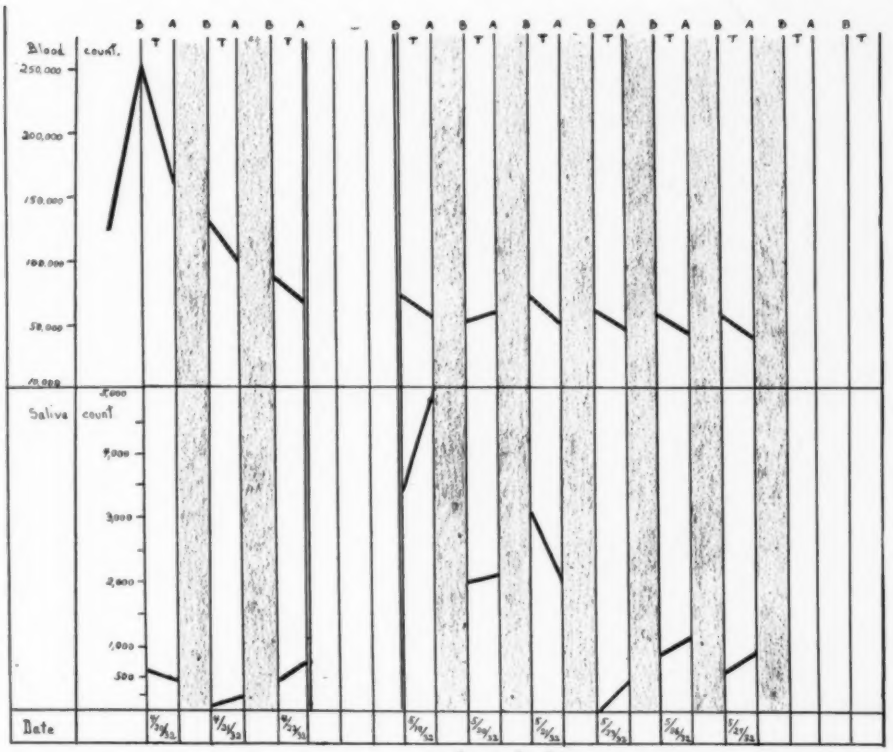
REPORT AND DISCUSSION OF CASES

CASE I. An obese male, aged forty-seven, first complained of progressive weakness and dizziness. This developed into a severe vertigo (Case VIII also presented this symptom). Headache became a prominent symptom. These three symptoms increased for a period of seven months, during which time there was an onset of multiple joint pains. A routine blood count disclosed the diagnosis and he was referred for roentgen treatment. Dyspnea and palpitation became distressing and epistaxis threatened his life. He also complained bitterly of visual disturbances. Ophthalmoscopic examination disclosed edema and hemorrhage of the retinae. There was also hemorrhage into both eyelids. Asymmetrical bone shaft tenderness was discovered. After a redious course of therapy (Figs. 3*a*, 3*b* and 9) a remission was finally secured. It was short and less than 50 per cent efficient and was terminated by chills and fever increasing in severity and frequency. In less than two months, the patient required hospitalization because of almost daily chills and fever which went to 105° F. He developed extreme pain and tenderness in the left upper quadrant over a huge spleen. A clinical diagnosis of splenic abscess was made. A pyelogram which indicated a structurally normal left kidney strengthened this opinion, although anuria had developed. During this time the leukocyte count mounted rapidly. A second series of roentgen treatments was initiated and effected some improvement. The leukocyte count reached a low of 19,750 (Fig. 6). At this time, however, daily differential blood studies revealed the appearance of more immature cell types than had hitherto been demonstrated (Fig. 8). Myeloblasts were present and increased in percentage as follows: 11, 15, 21 and 22 in daily counts. Ten days later the smears showed 45 per cent of myeloblasts. This made it mandatory to discontinue irradiation. The patient's condition rapidly became worse. Irradiation was employed again as a measure of last resort. Following two small exposures the leukocytes mounted from 56,000 to 220,000. Myeloblasts increased from 45 to 75 per cent and many dividing forms were seen (see Fig. 3*b*). These blood findings strengthen the opinion that irradiation applied in the presence of certain types of myeloblasts causes division instead of maturation and thereby increases the total number of cells. This case showed the lowest degree of efficiency after treatment, the shortest duration of life and the most discomfort of any in this group.

CASE II. Female, aged fifty-two. This patient noticed an enlargement in her left abdomen six months before we saw her. A month thereafter she visited her physician who quickly diagnosed myelogenous leukemia. Because the patient was still quite efficient in spite of an abnormal blood count, he rightfully did not refer her for irradiation until five months later when she had become inefficient as the result of the following conditions: pain in the left upper quadrant, abdominal pressure, dyspnea, gastroenteritis, burning sensation in both shoulders and purpura. She responded well to the first series of irradiation. Her blood and saliva cell counts showed reciprocal relationship. She is now experiencing a remission permitting high efficiency.*

CASE III. Female, aged twenty-nine, sought medical advice for a "lump" in her left abdomen and multiple recurring joint pains. The abdominal mass had been present at least seven months but was not reported because of a belief in Christian Science. She had, however, submitted to tonsillectomy, which was complicated by severe postoperative hemorrhage, for relief of her "rheumatism," two months prior to her discovery of the enlarged spleen. A month before this she had been donor of

* Patient still efficient, Jan. 16, 1937, two years four months following her first series.


B A B A B A

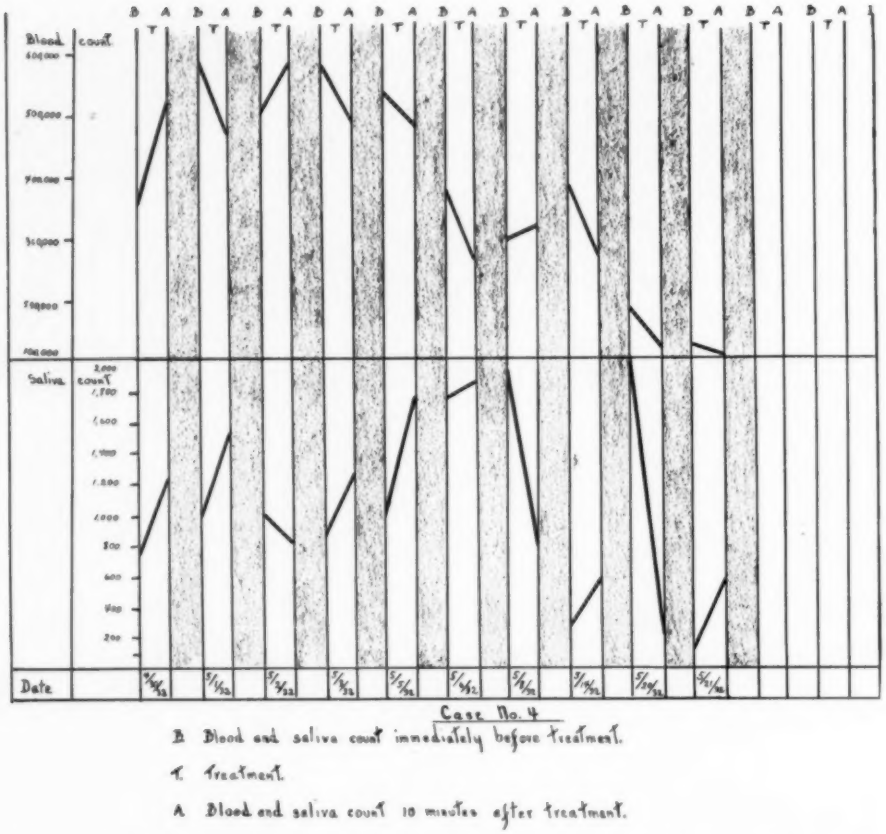

B A B A B A B A B A B A B A B A B A B A B A B A B A
Blood count
Saliva count
Date
Case No. 4
B Blood and saliva count immediately before treatment.
T Treatment.
A Blood and saliva count 10 minutes after treatment.

FIG. 5. The usual initial rise and inverse relation of saliva cell count to white blood count are present. The peak in saliva white count corresponds with the decline of initial white blood cell peak. A second high point in the saliva curve again matches a sharp drop in white blood cells.

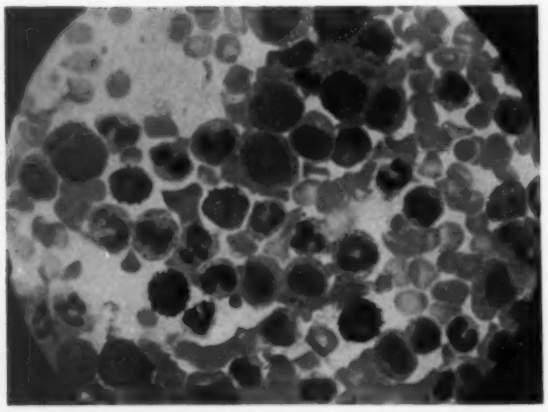


FIG. 6. Typical blood smear in chronic myelogenous leukemia from Case I. Irradiation at this stage stimulates a shift to the right (maturation) beginning with myelocyte (see Fig. 8). The total count decreases.

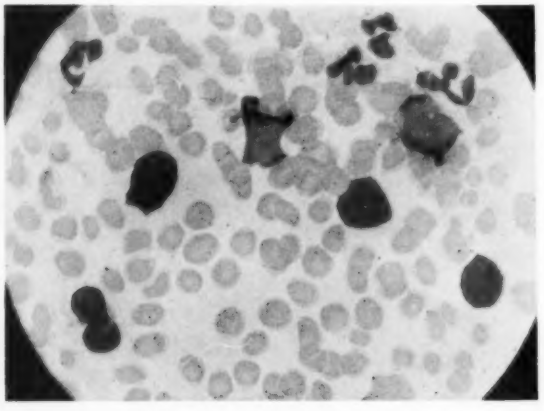


FIG. 7. Terminal stage of Case VII. Disintegrating basket type of cells and myeloblasts. Note also one dividing myeloblast. The intermediary granulocytes have matured. Irradiation at this stage increased the total count and the percentage of myeloblasts.

blood for transfusion to one of her two small daughters. She was undoubtedly suffering from leukemia at the time of transfusion. The child appears to be normal in every respect at this time, nine years later. We have found but one record of a leukemic patient donating blood for transfusion. The recipient will be kept under observation as long as possible. Purpura and joint hemorrhage accompanied by severe pain and stiffness were outstanding symptoms in this case. Graphs depicting the leukocyte counts of both blood and saliva are shown in Figures 2 and 14.

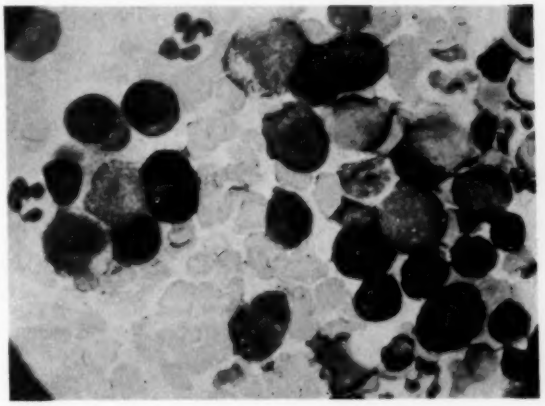


FIG. 8. Blood smear from same case as Figure 6 taken a few days before death. The two extremes of the life cycle of the granulocyte are present. Dark staining myeloblasts predominate with a few adult polymorphonuclear forms. Irradiation given at this stage increased the total count and produced division. Note dividing forms shown here (see Fig. 3*b*).

CASE IV. A large male, aged forty-one, presented himself to his family physician complaining of severe priapism of two weeks' duration. A careful examination revealed the cause to be chronic myelogenous leukemia. The priapism which lasted three weeks was accompanied by spells of anuria, lasting as long as forty-eight hours. Fifteen months ago the patient began to have occasional nose-bleeds and pain in left upper quadrant of his abdomen. These symptoms continued intermittently until roentgen treatment was instituted. Charted blood and saliva studies are shown in Figure 5.

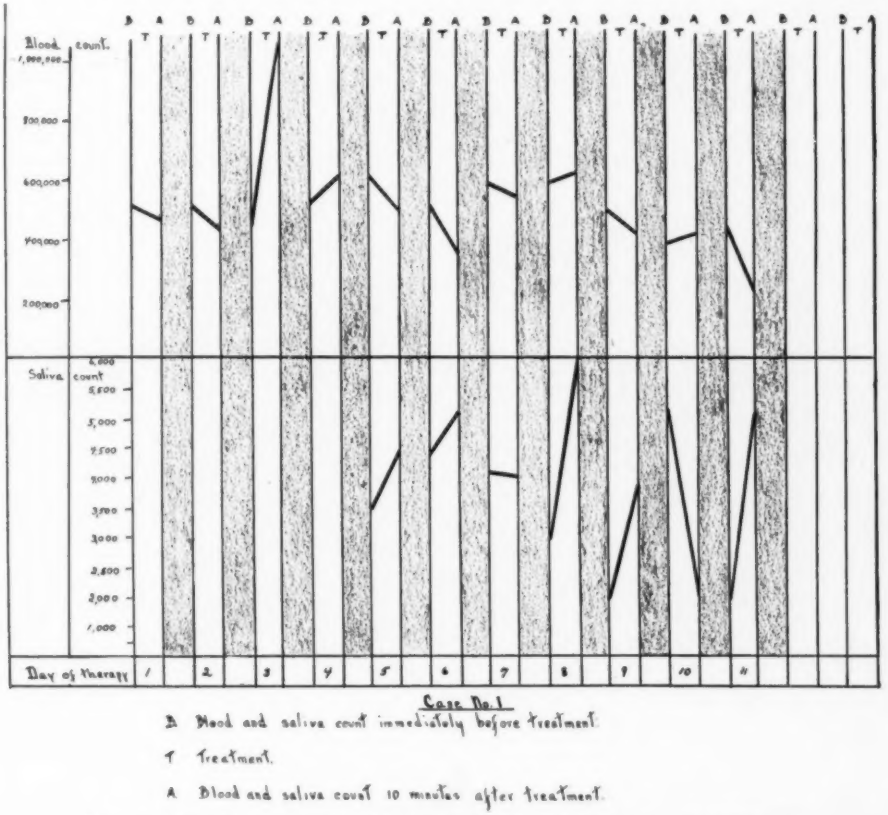

Blood count
Saliva count
Day of Therapy
Case No. 1
B Blood and saliva count immediately before treatment
T Treatment.
A Blood and saliva count 10 minutes after treatment.

FIG. 9. Another example of inverse blood and saliva count changes.

CASE V. A thin female, aged thirty-seven, who had experienced spells of diarrhea for years which her physicians told her were due to amebic dysentery. In April, 1931, she began to have "rheumatism," especially in one knee. She also noticed a large lump in her left

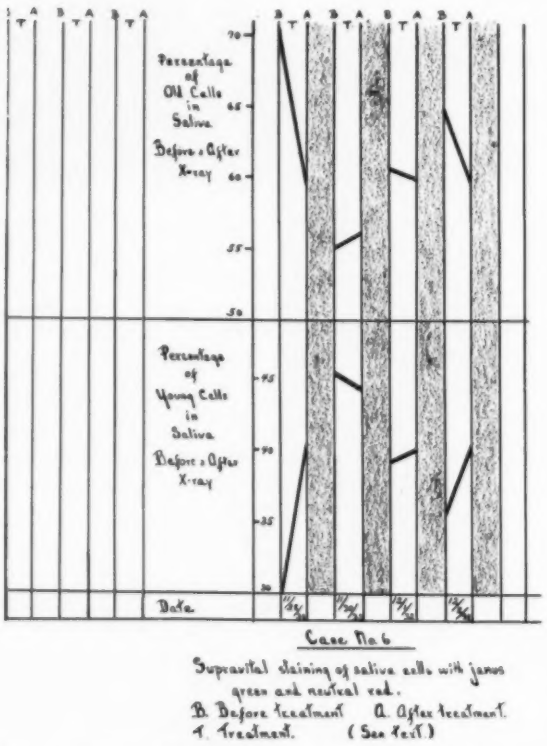

Percentage of Old Cells in Saliva
Before & After X-ray
Percentage of Young Cells in Saliva
Before & After X-ray
Date
Case No 6
Supravital staining of saliva cells with janus green and neutral red.
B. Before treatment A. After treatment
T. Treatment. (See text)

FIG. 10. Note that three times in four tests there was a higher percentage of young cells present in the saliva after irradiation than before. This is suggestive of a change in mouth mucous membrane threshold of leukopedesis.

abdomen a few months after the onset of the "rheumatism." A diagnosis of chronic myelogenous leukemia was made and irradiation was given in California during November and December, 1931. Only fair efficiency was obtained. The patient came to Colorado and was first seen by us in April, 1932, and found to be in urgent need of more treatment, essentially because of the large size of her spleen. Her response to irradiation was sluggish. After extraction of several infected teeth she improved without further irradiation.* However, she reported on November 8, 1932, complaining of splenic pressure; her blood leukocytes were 176,800 and saliva leukocytes 935. A series of roentgen treatments reduced the spleen only moderately; her blood count, however, became normal. Splenectomy, for comfort only, was advised and performed Feburary 1, 1933, with uneventful recovery. The spleen was eight times normal weight. A letter from the patient May 3, 1934, described her great relief from splenic pressure. An interesting series of supravital blood counts and saliva studies on this case made by Dr. G. Z. Williams will be described later. The patient was quite comfortable until the winter of 1934–1935 when increasing weakness influenced her to seek further irradiation. This was instituted and reduced the blood leukocytes only from 668,800 to 216,000. At this stage more premature cells appeared in the blood stream and the saliva cell count became atypical. This indicated that the marrow cells were exhausted and that further irradiation would be futile. The patient died in February, 1935. Blood and saliva leukocyte counts are shown by graphs in Figures 4*a*, 4*b*, and 14.

CASE VI. A female, aged forty-three, a court clerk, was first aware of indisposition when she discovered a mass in her left upper quadrant. This, she states, was present more than one year before she consulted a physician (patient is a Christian Scientist). She sought medical aid only after the advent of the following signs and symptoms: swelling of the extremities, pain in the abdomen, tachycardia, development of goiter, weakness, sweating and loss of weight. When the patient was referred to our roentgen department she was bedfast in the hospital. A period of remission was obtained quite readily to about 90 per cent efficiency. She has had two series in twenty months. The relationship between the blood leukocyte count and the saliva leukocyte count is shown in Figure 11.

CASE VII. A male, aged forty-three, first noticed an enlarged spleen in 1924. No roentgen treatment was given until 1927. He was treated in California and Rochester, Minnesota, before treatment in Denver, which was begun in 1928. He responded well to all series of treatments, reaching practically normal efficiency after each one. In 1927 infected tonsils and one apical dental abscess were found but not removed. We advised having these two sources of infection treated at a time of maximum ef-

* The effect of focal infection on myelogenous leukemia will be discussed in another communication.

ficiency and permitted him to return home. He was advised to report to us in one month for determination of his condition. Tooth extraction and possible tonsillectomy were contemplated if his condition was at a peak but he failed to return. Later at the time for another series of treatments when his condition was poor, his local physician permitted tooth extraction. This was followed by direct infection of the collateral maxillary sinus through a defect formed in the floor of the antrum. The blood stream quickly showed many myeloblastic forms which only increased in number with irradiation (Fig. 7). The patient only survived a few weeks.

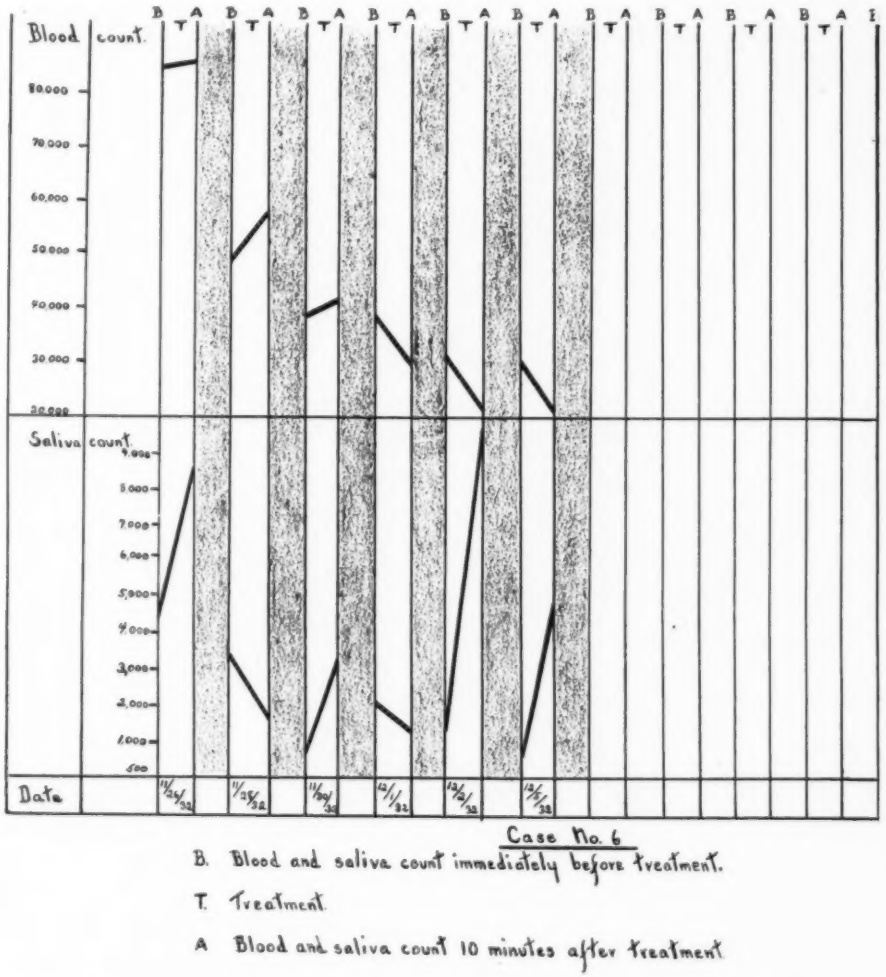


Fig. 11. Note the very active saliva response even though the blood count is low (see legend Fig. 4*a*).

Case viii. Female, aged forty-two. Ten months ago she noticed "swelling of her abdomen" and dyspnea upon mild exertion. It became necessary for her to go to bed each afternoon. Gaseous abdominal distention and increasing constipation developed. Recently she has lost weight and suffered from pain in her legs and back and has experienced some vertigo. One item of her past history is recorded. Four years ago she contracted malaria which has caused chills and a febrile reaction during the summer months. Since malaria has been used as treatment for myelogenous leukemia this portion of her history becomes interesting. Irradiation caused prompt and average blood leukocyte response and the usual reciprocity between blood and saliva leukocytes. She is now in a remission of high efficiency.

Case ix. Female, aged fifty-eight. She had been in failing health for two years. About five months ago her local doctor placed radium on the skin over a tumor in the left abdomen. He repeated this procedure four months later. The patient reported that the only result was a "sore" on the skin where the radium had been. The tumor did not subside so she changed doctors. The new physician, who found a total white count of 355,000, referred the patient to us. The spleen was 4 inches below the umbilicus and reached the midline of the abdomen. There were two scars on the skin, presumably the result of the radium applications. The blood and saliva count relationship is shown by graph in Figure 13.

Fig. 12. The outer line shows the size of the spleen before radiation therapy. The inner line shows the decrease in size before the spleen was treated, secondary to treatment of the long bones only.

Case x. A greatly emaciated male, aged sixty. Ten months ago he experienced serious hemorrhage on two occasions following the extraction of teeth. Shortly after he had recovered he noticed a "lump" on his left side. Four months before we saw him he became weak, began to lose weight and suffered severely from pains in the "bones" of his arms and legs. These symptoms gradually became more severe. The past history is interesting because he had submitted to treatment for "anemia" eight and six years ago. One year ago diarrhea caused him to seek medical advice and he received a diagnosis of amebic dysentery (see Case v). The first series of irradiation caused the average reciprocal blood and saliva leukocyte counts and remission was obtained in the average time.

Practical and Theoretical Considerations

Blood and Saliva Counts. Data obtained from this group of cases, part of which are recorded in the charted blood and saliva counts (Figs. 2, 3*a*, 3*b*, 4*a*, 4*b*, 5, 9, 10, 11, 13, 14), support Isaacs' belief that the appearance of more mature leukocytes in the circulating blood (shift to the right) which follows irradiation in this disease is the result of maturation of the white blood cells beginning at the stage of the myelocyte. The inverse relationship between changes in blood and saliva counts and the consistent decrease in the percentage of myelocytes resulting from irradiation found in our cases constitute strong evidence that roentgen-ray energy induces maturation of the myelocytic stage. The blood of Cases i and vii (see reports above and Figs. 7 and 8), studied during the last few days of life also supports his opinion that irradiation causes myeloblasts to divide instead of mature, rapidly increasing their number. Williams* in supravital studies of fresh blood from our patients during this stage demonstrated to us active division which was followed under the microscope. In two recorded observations the period required for completion of division was approximately thirty minutes. Irradiation, therefore, at a time when these cells dominate the blood picture is useless and probably harmful because it may not only crowd the blood with abnormal cells (Fig. 3*b*), but may also permit the bone marrow to pack and thus contribute to anemia by mechanically obstructing erythropoiesis.

Charts of Case iii (Figs. 2 and 14), also uncharted blood and saliva counts in Case v, present evidence that failure of the

* George Z. Williams, M.D., unpublished work.

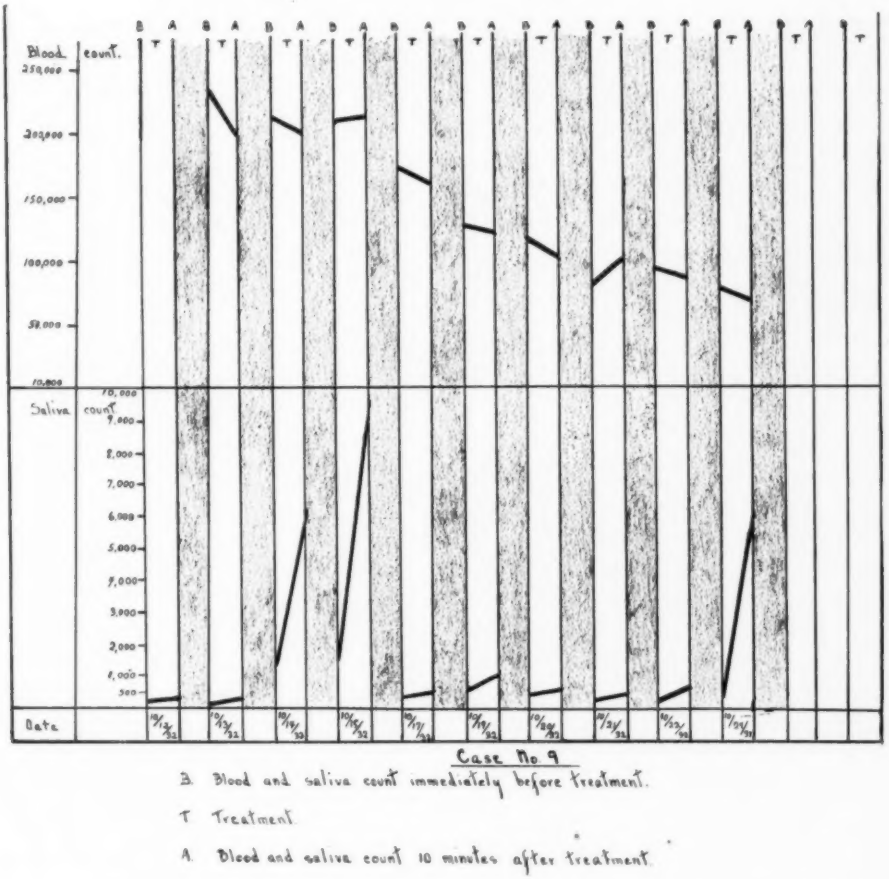


FIG. 13. Shows the inverse changes of blood and saliva counts brought about by irradiation (see Figs. 1, 2, 3*a*, 4*a*, 4*b*, 5, 9, 10, 11, 14). Throughout this series the large saliva cell count changes immediately after irradiation have resulted from treatment over spleen and mediastinum. Therapy over the long bones caused smaller changes (see text).

saliva cell count to increase following adequate irradiation suggests exhaustion of the marrow cells. When these cases reached the stage where the saliva counts remained low in spite of thorough irradiation, they also showed little clinical improvement as a result of the current series of treatments. Death followed in a few weeks in both cases. All previous series of treatments throughout six and four years, respectively, had raised efficiency remarkably in each case. These were the only series of treatments in each of these cases to show a poor saliva count response.

Maturation of myelocytes and division of myeloblasts is probably not the only effect that roentgen-ray energy produces in myelogenous leukemia. It will be noted in the graphs illustrating this article that initial treatments generally cause a temporary, often quite high, rise in the leukocyte count over a period of several days. The saliva count during this time also fails to respond by an immediate increase. An initial rise in blood leukocytes took place in Cases I, II, III, IV, V, VI, VIII and X. A failure of the saliva count to rise immediately occurred in Cases III and V (Figs. 2, 4*a* and 14) and only the slightest immediate rise in Cases I and IX (Figs. 3*a* and 13). As soon, however, as the saliva count mounts, the blood leukocytes rapidly decrease in numbers. Does this post-irradiation decrease depend not only upon matu-

ration to make blood leukocytes transmissible through the gastrointestinal mucous membranes, but also upon a changed membrane threshold to leukopedesis thereby permitting younger white cells to reach the saliva? An experiment represented by Figure 10 suggests that it does. A study of this chart shows that supravital staining subsequent administration over the same region. Yet the saliva response does not correspond as it should if maturation to old age were the only factor in the saliva count increase. Is this because the upper gastrointestinal mucous membrane requires irradiation to change its threshold before leukopedesis reaches its maximum?

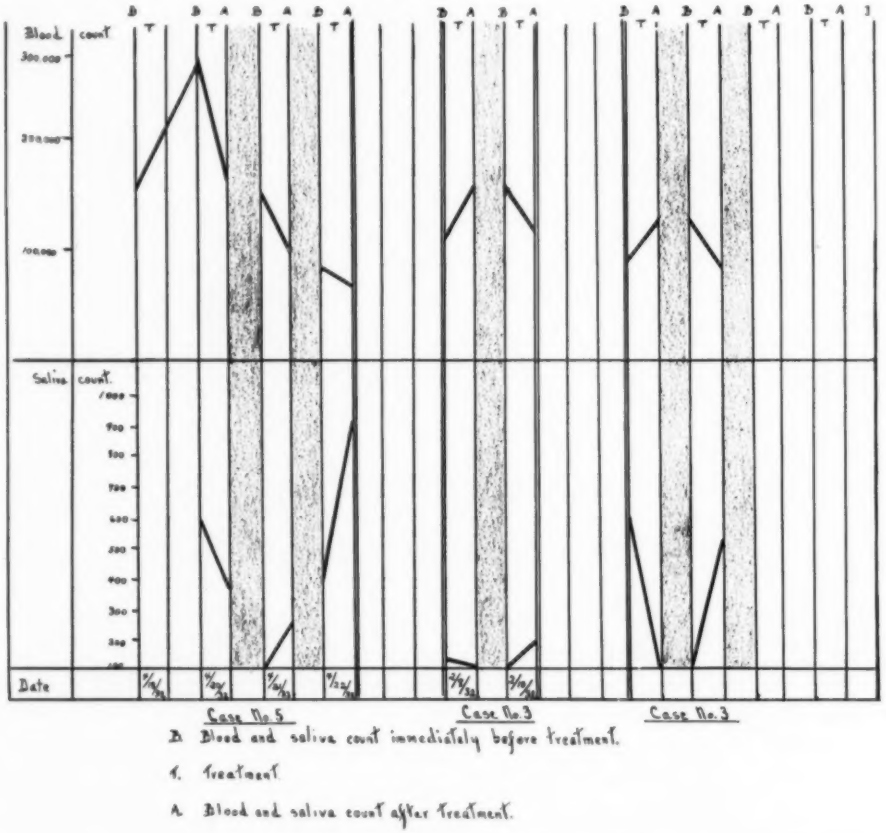


FIG. 14. Blood and saliva count relationship at different treatment series on same cases as shown in Figures 2 and 4*a*.

of saliva cells by Janus green B and neutral red reveals a higher percentage of young saliva cells after irradiation than before irradiation. Williams has made similar observations in his supravital studies. A change in the mucous membrane threshold which permits younger white cells to pass through it must be suspected. We find still further evidence which points in this direction. Surely an initial roentgen treatment produces as much maturation effect on the moving blood stream as This structure receives only secondary radiation and thus may require several doses before it is affected sufficiently to permit active leukopedesis. Throughout our group of cases leukopedesis was more active when treatment was given to the spleen and mediastinum (Fig. 13). It may be that the proximity of these areas to upper gastrointestinal mucous membrane, thus affording it more scattered radiation, is a factor as well as the obvious fact that greater blood volume is irradiated when

treating the spleen and mediastinum.

Case III showed a sudden terminal status in which irradiation failed to increase the saliva count. Since the length of the life cycle of the myelocyte is relatively short the cells present at the last series of roentgen treatments had never before received irradiation and therefore should not be radioresistant. Possibly the gastrointestinal mucous membrane had become resistant to its effect and the threshold failed to change.

Does myelogenous leukemia raise this threshold and lower the marrow-blood stream threshold? Does the unknown etiological factor in agranulocytopenia lower the upper gastrointestinal threshold, thus depleting the blood stream by permitting too ready exodus of the leukocytes finally exhausting the marrow cells? Certainly the early and frequent ulcerations and inflammation of the upper gastrointestinal mucosa in agranulocytopenia suggests that the membrane is subjected to some specific influence. Would this concept explain why very small doses of roentgen radiation over limited portions of the long bones prove beneficial in this disease by aiding maturation and doses large enough to reach the gastrointestinal mucous membrane secondarily result disastrously? These questions seem to open a wide field for further study.

Throughout our cases of leukemia blood slides demonstrate disintegrating myelocytes (Fig. 8). They appear too frequently to be ignored. The suggestion has continually intruded into the evidence that at certain stages of maturation under unusually heavy dosage or in certain particularly vulnerable areas of treatment, such perhaps as short wave length therapy over the liver region which we have used with benefit in 2 cases, irradiation may hasten the death of myelocytes instead of promoting their maturation.[18] Relatively larger numbers of apparently disintegrated myelocytes occur in the blood smears following a series of treatments than prior to therapy. This was especially true in Cases I, III and VII. This may be a factor in accounting for the occasional lowered blood leukocyte count without a compensatory rise in the saliva cell count. Examples of this can be seen in the following graphs: Case I, Fig. 3*a*(11/16/31), Fig. 9, (7th day); Case IV, Fig. 5 (5/20/32); Case V, Fig. 4*a*(4/20/32—5/21/32), Fig. 14 (4/20/32); Case VI, Fig. 11 (12/1/32). Isaacs* accounts for these disintegrated cells on another basis. He believes that some of those cells which are matured by irradiation in the blood stream where the acidity is represented by pH 7.4 with an unlimited amount of absorbable water reach a size which causes them to undergo traumatic disintegration in the process of making blood smears.

Much has been said about the saliva cell count. A summarization here of the practical application of this laboratory test to the management of myelogenous leukemia is appropriate.

The saliva count is the determination of the number of leukocytes per cubic millimeter of saliva. Leukocytes find their way into the oral cavity through its mucous membrane. They are absent in saliva collected directly from the salivary ducts and abundant in washings of the oral mucous membrane from which saliva has been excluded. Isaacs and Danielian[12] determined that 5 to 150 leukocytes per cubic millimeter of saliva is an average count for the normal individual. Isaacs' method of making a saliva count as used in this study is as follows: ask the patient to swallow, dry the mucous membrane of the mouth and tongue gently with gauze and rub the tip of the white cell pipette back and forth over the surfaces of the mucous membrane while exerting mild suction. The specimen thus obtained is counted in a blood cell counting chamber.

The saliva count furnishes information which becomes almost indispensable to the efficient management of a case of myelogenous leukemia. Persistent failure of the cells in the saliva to increase in numbers

* Personal communication.

ten or more minutes after irradiation suggests exhaustion of the marrow hematopoietic myeloblasts and is evidence that a poor response to the current irradiation series is to be expected. It might also be a sign of the onset of a myeloblastic state of the leukocytes in the blood stream and an existent or threatened erythrocytic dyscrasia. A prompt rise in the saliva count, on the other hand, probably indicates a healthier condition of the marrow cells and forecasts a good result from the current series. Further study may show that the response of the saliva count to irradiation is an appraisal of the condition of the blood stream-gastrointestinal threshold.

Management of Irradiation. The conception of the effect of irradiation as discussed thus far and presented in the charts helps to formulate indications and contraindications for beginning and ending a new series of treatments. Some of our studies show the relation of blood and saliva leukocyte counts following treatment to designated regions of the body. We believe that such charts made on a case at one series furnish a guide to the areas to be treated for optimum leukocyte response at subsequent series. This may be valuable in those cases in which difficulty is encountered in securing maximum simultaneous reduction of the spleen and blood count. It is now appropriate to consider the present status of management of roentgen treatment as outlined in recent literature and as modified by our observations. The details of dosage and technique are not necessary.

As a general rule, a series of treatments should be initiated only when the patient's general condition is poor and his efficiency low.[9,17] This applies to a newly diagnosed case which has never received roentgen treatment as well as to those which have had one or more series of treatments. The presence of large numbers of myelocytes, metamyelocytes and young polymorphonuclear leukocytes in the circulating blood, regardless of the total count, is considered by some to be sufficient evidence upon which to begin another series and undoubtedly is more important than the total count, but this alone even in the presence of a high total count does not necessarily indicate treatment. Only when these blood findings are combined with a high basal metabolic rate, sweating, nervousness, pains in the joints and other signs of hemorrhage such as its early manifestation in the retina and purpura, rapid pulse, loss of weight and appetite, any or all of which reduce the patient's efficiency to 50 per cent or lower, is treatment *indicated.*

A new series is contraindicated when the blood stream shows a great many primitive myeloblasts and myeloblasts[11] (Fig. 3*b*), especially if the saliva leukocytes persistently fail to increase following treatment. Even though a few myeloblasts appear in the blood smear, treatment can be continued as long as there is saliva cell count increase. Our Cases I and VII were treated in the presence of myeloblasts and the white count rose steadily and the patients immediately became worse. We believe that irradiation caused division instead of maturation and, as the blood stream became loaded with these abnormal cells, they also probably packed the marrow thus preventing red cell production by mechanical pressure. This accounts for the extreme anemia which rapidly ensued in these cases. Treatment is further inadvisable, even in the presence of a highly abnormal blood count, if the patient maintains efficiency and there is an absence of a syndrome of extenuating signs and symptoms. We believe also that irradiation should not be continued in the presence of a low blood count when treatment persistently fails to increase the saliva count, regardless of the patient's general condition.

SUMMARY

1. Blood and saliva studies and observations on a group of ten cases of chronic myelogenous leukemia confirm the belief that the major effect of irradiation upon the blood is maturation of the myelocyte to the polymorphonuclear stage and divi-

sion and reproduction of primitive myeloblasts and myeloblasts, as described by Isaacs.

2. Irradiation under certain circumstances and special dosage may cause death of some of the abnormal blood cells.

3. A little evidence which points toward an irradiation effect on the blood stream-gastrointestinal threshold of leukopedesis is presented.

4. A practical application of the recent conception of blood and saliva studies to the treatment of myelogenous leukemia is made.

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CENTRALIZED CONTROL FOR ROENTGEN APPARATUS

By P. D. HAY, JR., M.D.
FLORENCE, SOUTH CAROLINA

SINCE all modern roentgenographic machines have their various controls conveniently placed on a single panel, it seems logical that controls for separate units of the accessory equipment should likewise be centralized. There is some advantage in having a machine of sufficient power to do rapid roentgenography in any of the roentgen rooms and a large machine in each room is not only very expensive but occupies considerable space. Where these rooms do not exceed three in number and where they are grouped together, one machine is capable of doing the work satisfactorily, provided its available power can be rapidly changed from one room to the other. This seems reasonable when one considers the relatively short exposure time compared to the time consumed in positioning the patient, adjusting the apparatus, placing the cassettes, etc. A centralized control system which not only delivers the high tension current where used but controls all accessory equipment and furnishes a direct-reading milliampere adjustment has been used by me with entire satisfaction for the past two years. This system which I have designed and constructed is herein decribed.

The centralized control system consists of (1) the selector switch, (2) the robot for throwing the high tension switch, (3) the fluorographic unit, (4) various magnetic triggers, (5) Potter-Bucky exposure timing switches and (6) the milliamperage control.

The Selector Switch. The selector switch (Figs. 1, 2 and 3) for the installation under consideration consists of four sets of contacts of eleven points each, two collector rings and a suitable switch arm for connecting these. As indicated in the wiring diagram (Fig. 3), the four rows of contacts from above downwards control the following respective circuits: (1) robot for throwing the high tension switch, (2) filament circuit, (3) foot switch and Potter-Bucky timing connections and (4) magnetic trigger controls. The switch arm makes connection between one contact of each row at a time and each collector ring by means of multiple phosphor bronze strips, thus insuring good contact at all times. As shown by the heavy dotted line in the wiring diagram (Fig. 3) the switch arms supplying the two top rows and bottom row of contacts and the upper collector ring are connected together and this circuit represents the grounded side of the 110 volt A.C. line. Also switch arms connect the smaller of the lower rows of contacts with the lower collector ring which receives the other side of the line.

By means of the one selector switch, the operator is able instantly to secure any one of nine combinations of controls which involve five separate circuits. In my installation only six combinations are being used, others being kept in reserve. Since the one machine is used in three different rooms, the switch positions are divided into three major groups and these divisions correspond to the three rooms: roentgenographic, roentgenoscopic and cystoscopic. These divisions as well as subdivisions are marked on the panel (Fig. 1) covering the switch.

Robot for High Tension Switch. For the operator's convenience the high tension switch is swung into any of its three positions by a robot which is controlled in turn by the selector switch. The robot was removed from its regular position in order that its mechanism might be photographed. In use this mechanism is encased to protect it from dust, is mounted on the wall opposite the high tension switch and the toothed universal joint

(Fig. 4) is connected with the shaft of the high tension switch by means of a bakelite rod 2 feet long.

Figure 4 shows the robot mechanism which consists of a small motor, a speed reducing gear, reversing cams, a reversing relay and a magnetic brake. The motor is one designed for sewing machines. The gear box houses an oil-immersed double worm gear with a reduction of 100 to 1. The reversing relay was made from a pole-changing radio jack with the addition of two solenoids to shift it. Two cams were constructed from bakelite discs, of shapes shown in the wiring diagram (Fig. 3) and these were attached to the same shaft which swings the high tension switch. These cams actuate two single pole, double throw switches as shown. Their position indicated in the wiring diagram corresponds to the middle position of the high tension switch. While the larger cam serves to break the circuit at each end of the swing, the smaller, working in combination with the three leads from the selector switch and the reversing relay *C*, determines the direction of rotation of the motor, *D*, or stops it in the middle position. The magnetic brake, *E*, is set by a spring as soon as the current ceases to flow, thus preventing "coasting" of the switch.

Fig. 2. Control box with panel removed to show internal mechanism.

Fig. 1. Control box with panel in position.

The Fluorographic Unit. The fluorographic unit, which I constructed nine years ago and which has been in use ever since, is a very simple affair. Placed within easy reach of the operator in all positions of the roentgenoscopic table, the assembly is mounted on the right leg of the roentgenoscopic table. As shown in Figure 5, the unit is housed in three switch boxes of standard size placed end to end and covered with a single bakelite plate.

The upper box holds an ordinary wall switch which is connected to the green ceiling light. Within the middle box is mounted a double pole, single throw tumbler switch of 20 ampere capacity. A small fan motor was rewound and cut down to

fit in the lower box. The armature was wound in one plane and the two leads brought out by very flexible wire run through soft rubber tubing. This device serves as a variable reactance represented by *F* in Figure 3. By means of a handle mounted on the shaft end (Fig. 5) the armature can be rotated through 180 degrees. With the handle straight down the armature and field coils work together giving sufficient reactance to lower the milliamperage to 1.5. When the handle is turned up the magnetic effect of the armature bucks that of the field so that the filament current is raised to produce a 6 ma. flow through the tube. At these milliamperages the stabilizer when set on 30 ma. fails to work so that for roentgenoscopy the milliamperage is under direct control by the fluorographic device.

Instant change from the roentgenoscopic setting to the roentgenographic is accomplished simply by throwing the double pole switch in the middle box. This switch (*G*, Fig. 3) short circuits the variable reactance allowing the stabilizer to function at its setting of 30 ma., and at the same time short circuits all resistance up to button 16 on the transformer resistance control. This delivers 30 ma. at 85 kv. (peak).

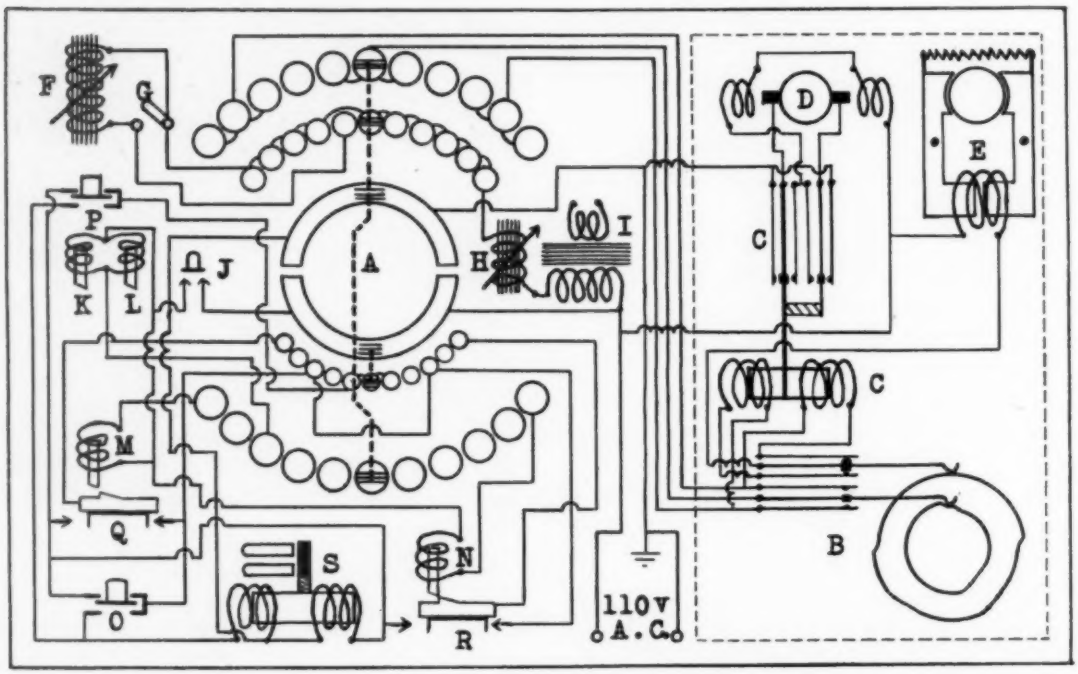

Fig. 3. Wiring diagram. Dotted line in right section incloses circuit for high tension switch robot. *A*, center of selector switch. *B*, cams and their switches. *C*, reversing relay. *D*, motor. *E*, magnetic brake. *F*, variable reactance. *G*, fluorographic switch. *K*, *L*, *M* and *N*, magnetic triggers. *O*, foot switch in control room. *P*, foot switch in roentgenoscopic room. *Q*, Potter-Bucky contacts in main roentgenographic room. *R*, same in cystoscopic room. *S*, magnetic relay for main transformer.

Magnetic Triggers. Magnetic triggers on moving parts of accessory equipment not only save time and eliminate the annoyance of having to untangle strings but do away with the shaking of the apparatus which often follows the jerking of a string. While most stereoscopic cassette changers and tube stands are provided with magnetic triggers, Potter-Buckey diaphragms usually are not. These triggers can be made at small cost by placing a suitable winding on the center leg of the core obtained from a small radio trans-

former and using the removable part of the core as the armature to pull the trigger. As shown in the wiring diagram (Fig. 3) four magnetic triggers are used in this installation. *K* and *L* are respectively triggers on the tube stand and cassette changer for chest roentgenography. Trigger *M* is located on one Potter-Bucky diaphragm and *N* on the cystoscopic Potter-Bucky. The push button *J* energizes whatever trigger is placed in the circuit by the selector switch. A variety of combinations may be made by connecting the triggers to suitable contacts on the lower row of the selector switch.

Potter-Bucky Exposure Timing Switches. Most Potter-Bucky diaphragms are provided with a switch for operating the transformer relay so that the exposure is automatically timed while the grid is moving. However, in the usual installation it is impossible for the operator to instantly stop the exposure in the event that the patient or some onlooker nears the high tension circuit. This can easily be arranged by connecting the Potter-Bucky exposure switch in series with a foot switch *O*, as shown in the wiring diagram (Fig. 3). *Q* and *R* represent Potter-Bucky switches on the two diaphragms respectively. These and the foot switches operate transformer relay *S*. As indicated in the circuit, each position of the selector switch represents its own combination of foot switch or Potter-Bucky control. This provides an additional safety feature, preventing energizing of the transformer by accidental closure of a foot switch in another room.

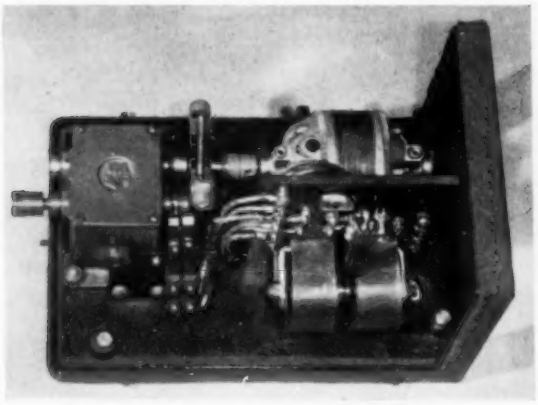

Fig. 4. High tension switch robot with cover removed.

Fig. 5. Fluorographic control with and without panel.

The Milliamperage Control. Obviously there is considerable advantage in being able to preset the controls for a given milliamperage by an adjustment which gives a direct reading. This is effected by manipulating the knob appearing on the upper center of the control panel (Fig. 1) until the desired milliamperage appears centered in the window above it. There extends back, from the knob mentioned, a shaft which is connected to the vertical stabilizer control by two bevel gears. Upon this shaft is mounted a small gear which engages with a larger ring gear bearing a circular piece of thick celluloid (Fig. 2). The upper part of this celluloid circle is backed by a stationary heavy brass support with a large hole cut in its lower end, the two being separated by about 1 mm. The control is calibrated periodically by removing the magnifying window (a kodak portrait attachment), turning the knob with tube running until the desired milliamperage is recorded on the milliammeter, then stamping this value directly on the celluloid circle by means of rubber stamps bearing an oil-base ink. The purpose of the brass support mentioned above is to furnish a solid

foundation for stamping pressure, thus preventing any bending of the ring mounting. Old figures can easily be washed off with carbon tetrachloride. After calibrating, the window is replaced and small figures, being magnified, are shown clearly by the pilot light behind the celluloid disc.

In order to change the scale reading on the milliammeter a control is provided for this purpose. The knob appearing on the upper left of the control panel (Fig. 1) is mounted on a plunger which is connected to a flexible steel wire, then a linen cord to the shunting switch on the milliammeter. By pulling the knob the scale is changed alternately to the high and low readings.

SUMMARY

A centralized control system of original design and construction is described and illustrated which has been used satisfactorily for two years and which facilitates the use of one machine to supply three separate rooms.

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VENTRICULOGRAPHIC LOCALIZATION OF INTRACRANIAL TUMORS*

I. TUMORS INVOLVING THE POSTERIOR PART OF THE THIRD VENTRICLE AND THALAMUS

By VINCENT C. JOHNSON, M.D., *and* CARL F. LIST, M.D.
ANN ARBOR, MICHIGAN

IT IS oftentimes difficult, if not impossible, to accurately localize brain tumors on the basis of clinical evidence alone. Clinical neurological examination may be expected to yield accurate localizing information in at least one-half of any diversified group of intracranial neoplasms,[1] but in the case of tumors situated in or near the posterior portion of the third ventricle, neurological signs are of lesser localizing value. This same situation obtains also in the case of many subtentorial tumors. Tumors in the first group may give rise to cerebellar signs sufficiently prominent to convince the examiner that the lesion lies beneath the tentorium, and, on the other hand, tumors of the posterior fossa may produce signs referable to the midbrain, an equally confusing situation. It is of no little importance to the brain surgeon and his patient that the exact location of an intracranial tumor be determined before operative procedures are begun. The brain surgeon's task, never an easy one, is rendered less difficult if before operation he can be advised of the extension of a cerebellopontine angle tumor into the midfossa. So important are these and kindred considerations that roentgenographic examinations which can provide such information enjoy wide usage.

Routine roentgenographic examination of the skull without the employment of artificial contrast methods is sometimes sufficient to provide all desirable information regarding a tumor. Deposition of calcium within the tumor itself in rare instances provides excellent localizing information. Observed vertical or lateral displacement of a calcified pineal body may be most enlightening, but for real accuracy in the matter of localizing tumors which arise beneath the tentorium or in the neighborhood of the third ventricle, the ventriculographic procedure is vastly more useful and reliable.

Since the value of information obtained by the study of ventriculograms is so directly dependent upon technical exactitude, both surgical and roentgenographic, it is necessary before entering into a discussion of ventriculographic signs to describe the steps necessary to produce reliable roentgenograms of this sort.

THE OPERATIVE TECHNIQUE OF VENTRICULOGRAPHY

Occlusive hydrocephalus, nearly always produced by tumors of the sort under consideration, simplifies the surgical aspect of ventriculography since the lateral ventricles, when dilated, are easily accessible to the aspirating needle through any silent area of the cortex. It is of paramount importance that maximum drainage of the ventricular system be accomplished. To this end, the head must be rotated in such a manner as to bring the point of the cannula into a dependent position with relation to all other parts of the ventricular system. In this clinic the following surgical technique is used:

Under local anesthesia, a short vertical incision is made at a point 4 cm. superior and the same distance posterior to the tip of the right ear. The parietal bone is drilled with a Hudson burr No. 3, and the dura is split in a stellate fashion. A blunt ventricular cannula is then aimed at the vestibule of the right lateral ventricle.

* From the Department of Roentgenology and the Department of Surgery, Service of Dr. Max M. Peet, University of Michigan, Ann Arbor, Michigan.

The cannula is then pushed through brain substance until the ventricle is entered. A normal ventricle lies at a depth of 4.5 to 5.5 cm.; a dilated ventricle is found at a lesser depth. Removing the stylet, initial intraventricular pressure is measured.

Drainage is now begun by means of a Luer syringe attached to the cannula with flexible tubing. Each 10 c.c. of fluid withdrawn is at once replaced with pure oxygen, exercising care to avoid the exertion of excessive pressure during the maneuver.* This procedure is continued until, instead of fluid, gas returns upon aspiration. The head is now rotated sharply toward the right to permit fluid from the dependent parts of the other ventricles to enter the right side via the foramina of Monro. When no additional fluid can be obtained, the cannula is withdrawn and the scalp wound closed with silk. Roentgen examination is begun immediately.

ROENTGEN TECHNIQUE

In this clinic nine separate roentgen exposures are employed in routine ventriculographic examinations. Stereoscopic technique is employed for right and left lateral projections and the anteroposterior sagittal projection. Single exposures are employed for the posteroanterior sagittal view and two additional lateral projections, the first with the forehead superior, the second with the occiput superior. In all but these last two exposures, the film is held in a horizontal plane, the head is supported beneath the film, and the exposure is made from below, permitting the inflated portions of the ventricular system to come in close proximity to the film surface. Target film distance is maintained constantly at 36 inches. By these means distortion is minimized.

All exposures are made with the use of a moving Potter-Bucky diaphragm. Factors of voltage and current routinely employed permit exposure time to be held at a maximum of two and a half seconds, at which speed it is possible to avoid troublesome motion.

Exactitude in the matter of positioning the head is tremendously important to accuracy of film interpretation. This is particularly true in the case of sagittal projections, for slight deviation from the exact anteroposterior axis deprives recognizable signs of bilateral asymmetry of their reliability.

Difficulties encountered in preparing exposures with a beam of roentgen rays directed from floor to ceiling are well rewarded in the ease with which one can orient anatomical landmarks with respect to photographic identification marks on films. He is always assured that the more completely aerated portions of the ventricular system are those which lie closest to the plane of the film, a point easily determined when stereoscopic vision is employed. The only exception to this rule occurs on those occasions when communication between the lateral ventricles is disturbed.

By and large, in the ventriculographic study of tumors involving the posterior portions of the ventricular system, the anteroposterior sagittal projection, occiput superior, and the lateral projection in a horizontal beam, with the occiput superior, will be found to furnish the most valuable diagnostic information. With the skull in these positions, residual fluid gravitates away from the areas requiring closer study, permitting the maximum degree of artificial contrast where most needed. It is not wise to rely entirely upon these particular projections, however, for one is often able to learn much of value from the other films, and is seldom able to afford the risk of foregoing any possible assistance they may render.

Brain tumors involving the posterior portion of the third ventricle, as well as those which lie beneath the tentorium, may be expected to produce striking degrees of hydrocephalus in the ventricular system

* At this clinic, it is felt that the substitution of oxygen for air constitutes a partial safeguard against untoward complications, for oxygen is absorbed from the ventricles at a rate almost equal to that of spinal fluid production and faster than that at which air is absorbed.

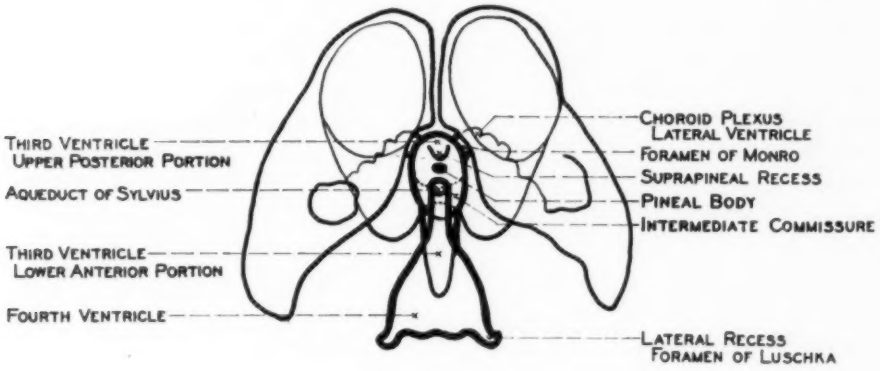


Fig. 1

anterior to the site of their location. The real purpose of the ventriculographic procedure, however, is to obtain detailed information regarding the exact site of the tumor, its position with regard to the midline of the brain, and, if possible, some conception of its size. To be sure, the degree of deformity and distention of the lateral ventricles and bilateral inequality of ventricular size are sometimes of importance in determining the size and location of tumors, but the really important evidence in such matters is gained from a searching study of visible landmarks in the immediate vicinity of the tumor itself. Only with much practice, first-hand experience regarding appearances at operation, and careful study of autopsy material, as well as an understanding of the anatomical basis of neurological findings can one hope to extract from ventriculograms the useful evidence which they provide.

Before attempting to discuss localized deformities of the third ventricle, it is necessary to describe the changes it undergoes as the result of simple dilatation. In the frontal sagittal projection, occiput down, it is seen as an oval space in contrast to its normal vertical slit-like appearance. Viewed in the sagittal plane with occiput superior (Fig. 1), it may be said to have two parts. The uppermost portion, which is rounded and very translucent, represents the superior and posterior part of the ventricle upon which is superimposed the suprapineal recess. The oval, less translucent, portion below corresponds to the lower part of the anterior segment including at its tip the infundibular recess. In both of these projections, a narrow shadow is to be seen crossing the middle of the third ventricle from side to side. This shadow represents the intermediate commissure.

As seen in the lateral view (Fig. 2), the third ventricle when uniformly dilated re-

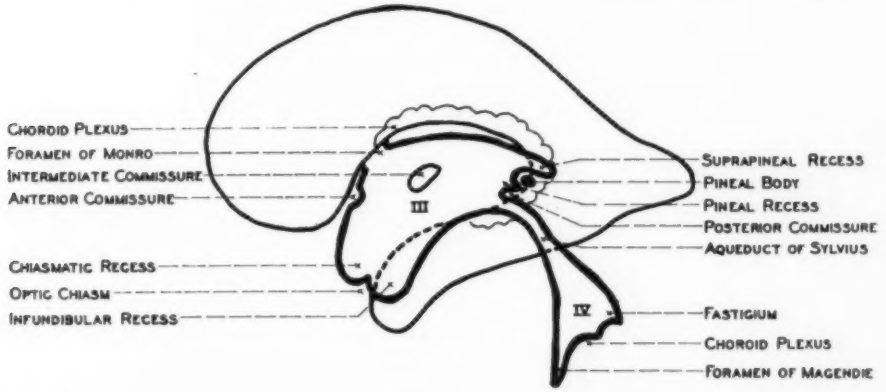


Fig. 2

veals the location of immediately adjacent structures by means of numerous recesses and indentations.

The somewhat complicated boundary contour can be conveniently divided into four quadrants: superior, inferior, anterior and posterior. The superior margin extends from the posterior edge of the foramen of Monro to the tip of the suprapineal recess posteriorly. The inferior margin begins anteriorly with the infundibular recess and extends to the anterior wall of the aqueduct. The anterior quadrant begins above at the anterior margin of the foramen of Monro, extending downward to the infundibular recess, while the posterior quadrant consists of a short, irregular border beginning with the tip of the suprapineal recess above and ending in the posterior wall of the aqueduct below.

The superior quadrant curves smoothly parallel to the floor of the lateral ventricle and represents the tela choroidea of the third ventricle. The pons, the mammillary bodies, and the infundibular portion of the hypothalamus give shape to the relatively smooth and curved inferior margin. The anterior quadrant is indented in its upper portion by the anterior commissure and at its lower end by the optic chiasm which produces a dividing ridge between the chiasmatic recess and the deep sacculation in close contact with the dorsum sellae known as the infundibular recess. The posterior wall of the third ventricle is very irregular. Above one finds the suprapineal recess extending posteriorly above the pineal body itself, while below the pineal body a smaller recess is found. The sharp curve of the ventricular border just above its junction with the aqueduct is produced by the posterior commissure. Slightly above the midpoint of the ventricle the intermediate commissure can be recognized as an oval shadow. When the degree of hydrocephalus is unusually marked, atrophy and stretching of the intermediate commissure may deform the shadow of this structure as seen in lateral view until it appears unusually small and narrow.

When the ventricular system is not abnormally dilated, lateral ventriculograms show no overlapping of the third ventricle by other gas-filled cavities. Lateral ventriculograms of hydrocephalic brains show to a considerable degree superimposition of lateral and third ventricles. Under these circumstances, the entire posterior and inferior margins of the third ventricle are projected within the boundary of the temporal horn. If, in the hydrocephalic brain, these portions of the third ventricle are projected above the temporal horn, as seen in lateral view, this finding indicates abnormal upward displacement of the brain stem.

Since July 1, 1931, approximately 400 proved brain tumors have been studied roentgenographically in this clinic. Tumors of nearly every type and description are presented in this group. From among those in which the tumor involved the posterior portion of the third ventricle, the ventriculograms of 9 have been selected to illustrate localizing signs of proved reliability.*

MIDLINE TUMORS

The tumors to be considered in this group are those which, by virtue of their site of origin, produce deformity of the posterior portion of the third ventricle and usually obstruct the anterior portion of the aqueduct without displacing these structures to either side of the midline. Such tumors may originate in the region of the pineal body, the posterior commissure, the region of the aqueduct, or from both thalami, and they produce ventriculographic changes which are most readily apparent in lateral projection. Characteristically, these midline lesions deform the posterior quadrant of the third ventricle. If the tumor is truly midline, the rounded indentation of the posterior quadrant produced by the tumor appears symmetrical in right and left lateral projections. The sagittal projection with occiput superior may show the tumor to be encroaching

* Two valuable articles dealing with the ventriculographic study of brain tumors[2,3] have appeared in print during the preparation of our communication.

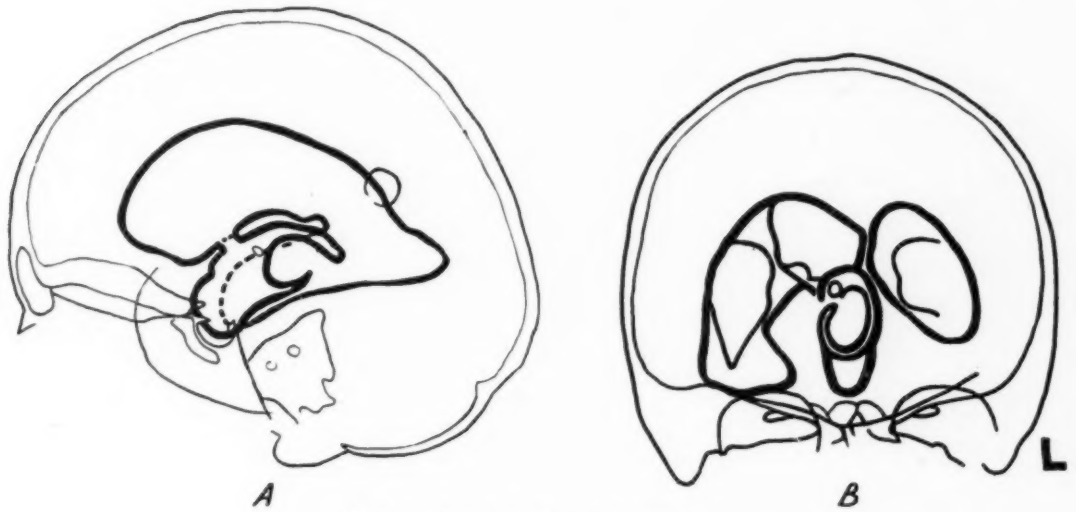


Fig. 3, *A* and *B*. Case 1 (355157).

upon the gas-filled ventricle, but the absence of lateral displacement of the ventricular system constitutes the chief value of this view in identifying tumors belonging to this group. Unless a midline tumor in this region of the brain develops to large size, it produces no visible distortion of the lateral ventricles other than generalized distention. Distortion of the lateral ventricles, directly due to large midline tumors, is characterized by symmetrical displacement away from the midline together with slight upward displacement. The sagittal view with forehead superior yields no additional localizing information in cases of this sort.

Observations derived from the study of 5 brain tumors exemplifying this particular midline group serve to demonstrate the various types and degrees of third ventricular deformity which one may expect to encounter. The first of these, Case 1, found at operation to be a teratoma lying within the dilated third ventricle, attached to the right lateral wall posteriorly by a small vascular stalk, is an excellent example of intraventricular tumor. In the lateral view (Fig. 3*A*) it is represented by the shadow of a ball-shaped mass encroaching upon the posterior part of the third ventricle without obliterating the suprapineal recess or the usual landmarks

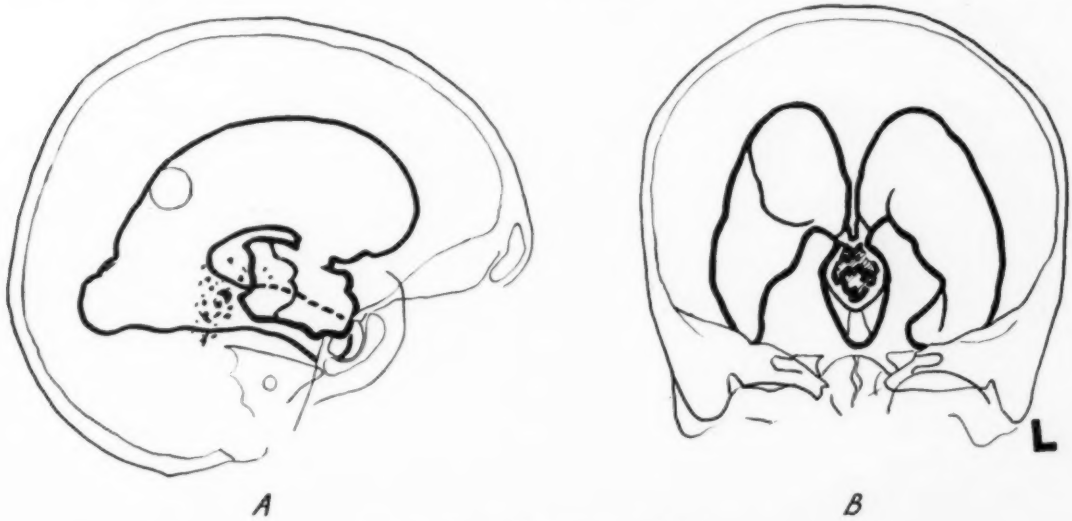


Fig. 4, *A* and *B*. Case 11 (346766).

Fig. 5. Case III (212050).

of the ventricular floor. The tumor is particularly well visualized in the sagittal projection, occiput superior (Fig. 3*B*), for here it is seen completely surrounded by a layer of oxygen except for the shadow cast by the pedicle on the right.

The pineal body, because of the frequency with which its exact location can be identified by virtue of physiological calcium deposits, may be said to constitute one of the common landmarks within the brain. Intracranial neoplasms arising in this body may on occasion be recognized because of included calcium deposits without the assistance of ventriculography. Observed by the ventriculographic method they present a striking appearance, as a rule, because of the relatively characteristic changes which they produce. These tumors are ideally located to produce obstruction of the aqueduct which lies almost immediately beneath the pineal body. Because the pineal is normally recessed in the posterior wall of the third ventricle, it may be expected that a neoplasm arising here will quickly encroach upon the posterior portion of the third ventricle. Since the pineal body is strictly a midline structure, pineal tumors are, as a rule, central in position, producing no lateral displacement of the ventricular system.

Case II represents a pinealoma of generous dimensions associated with typical clinical symptoms and signs and recognized in routine examinations of the skull by virtue of extensive, irregular calcium deposition within its substance. In the lateral ventriculogram, left side superior (Fig. 4*A*), the somewhat irregular anterior boundary of the tumor is seen to protrude into the third ventricle, effectively effacing the normal configuration of its posterior wall. The calcium deposits already mentioned correspond well to the soft tissue mass. In the sagittal view, occiput superior (Fig. 4*B*), all of the calcium deposits are seen to be clustered within the gas-filled space which represents the posterior portion of the third ventricle. The tumor is seen to be strictly midline in position. The lower margin of the tumor mass is sharply contrasted against oxygen within the ventricle.

Not all pinealomas reach sufficient size to completely obliterate the aqueduct before they are subjected to roentgenological examination. Occasionally, one encounters a tumor of this sort, the dimensions of which are small. The protrusion into the gas-filled third ventricle can still be recognized. Calcification, frequently present, is helpful in identifying the nature of the tumor, and the midline position, as seen in sagittal projection is, of course, highly suggestive of the tumor's identity. Case III represents a tumor of this sort successfully removed surgically following ventriculographic identification. The left lateral pro-

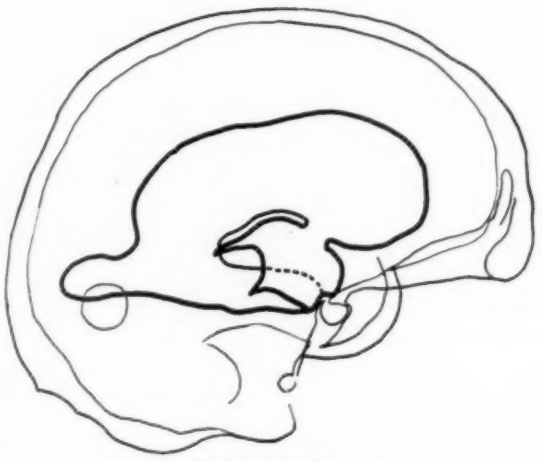
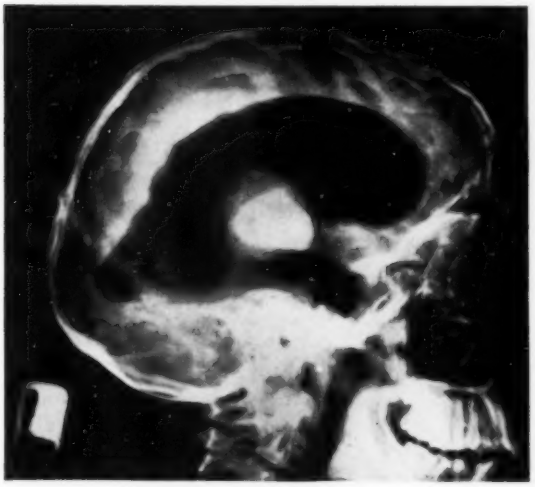


Fig. 6. Case IV (270355).

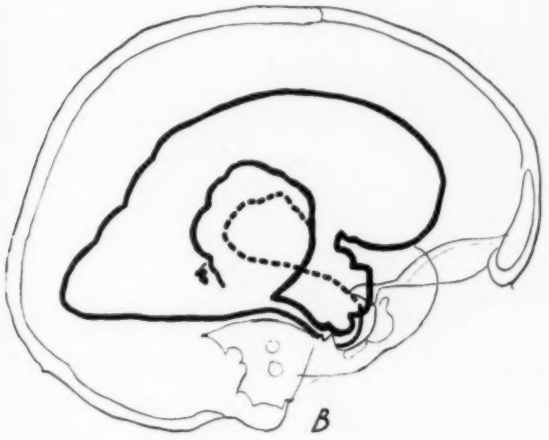
jection, occiput superior (Fig. 5), shows small scale but typical posterior quadrant deformity. A small calcium deposit is seen within the tumor. Partial gas filling of the fourth ventricle resulting from incomplete blockage of the aqueduct offers further evidence of the tumor's small size.

Another type of brain tumor which fits the general pattern of midline defects involving the posterior aspect of the third ventricle is the ependymoma. Case IV represents one of these tumors proved at operation as to site and microscopically as to type. Figure 6, lateral view, left side superior, shows a smooth, rounded, soft tissue projection into the gas-filled third ventricle deforming the posterior wall.

Thalamic tumors, sufficiently large to



A



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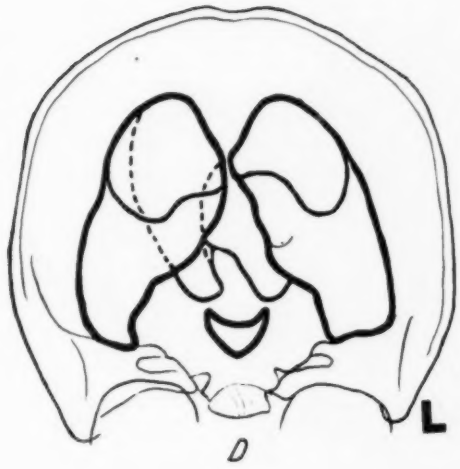


FIG. 7, *A*, *B*, *C* and *D*. Case V (350900).

involve both sides equally, may be considered with the midline group. Case v exemplifies the ventriculographic appearance of this situation, demonstrating not only the position of the tumor mass but also its relatively large size. This particular tumor was found at operation to be a huge astrocytoma. The lateral projection, left side superior (Figs. 7*A* and 7*B*), shows all but the most anterior portion of the third ventricle to be obliterated by soft tissue encroachment. The opposite lateral projection (not shown) is similar in all respects. The tumor is of sufficient size to indent the bodies of the lateral ventricles from beneath. Visible calcification of the pineal body seen posterior to and somewhat below the main mass of the tumor bears witness to the fact that this tumor arises anterior to the pineal body. In sagittal view, occiput superior (Figs. 7*C* and 7*D*), the lower border of the tumor is seen to be outlined by a crescent-shaped collection of oxygen in the lower anterior portion of the ventricle. Another index of this tumor's large size is found in the slight elevation and lateral separation of the lateral ventricles as seen in this projection.

Figure 8 *A* and *B* represents in schematic form a large pineal tumor as seen in direct lateral, as well as in sagittal view, comparable to the appearance as shown in lateral and sagittal ventriculograms, the latter made with the occiput superior. These drawings exemplify the main ventriculographic features of midline tumors in the region of the posterior part of the third ventricle. Deformity of the posterior wall of the third ventricle by anterior protrusion of tumor tissue, obstruction of the aqueduct by pressure from above, and the absence of lateral displacement of midline structures are the typical characteristics of tumors in this group.

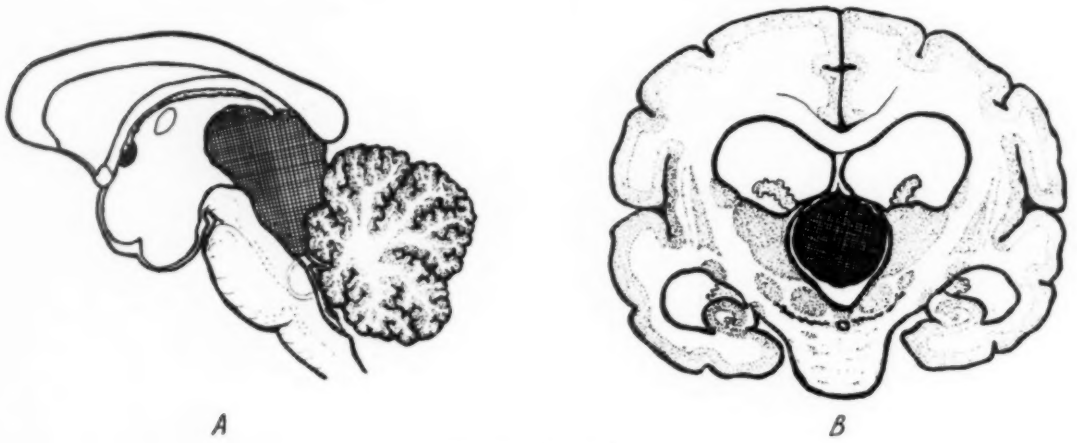


Fig. 8, *A* and *B*.

LATERALIZED TUMORS

Thus far, in considering tumors so situated as to deform the posterior aspect of the third ventricle, we have dealt solely with lesions lying directly in the midline. The ventriculographic signs which have been discussed are straightforward and relatively simple. Tumors arising to one side of the midline in close proximity to the posterior portion of the third ventricle produce ventriculographic changes which may be very bizarre and complex. In examining such films, it is not at all difficult for the observer to lose his bearing and fail to recognize reliable localizing signs even when these are present.

The basic anatomical changes responsible for roentgen signs of tumor lateralization may be listed as:

1. Unilateral soft tissue protrusion into the posterior portion of the third ventricle.
2. Displacement of the posterior portion

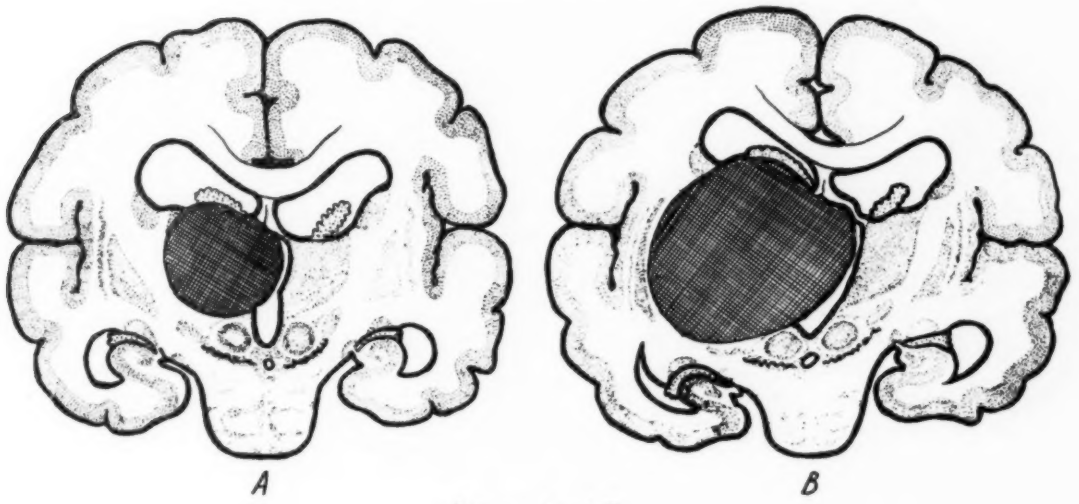


Fig. 9, *A* and *B*.

of the third ventricle away from the tumor side.

3. Compression of the body of the lateral ventricle on the affected side and elevation of its floor.
4. Downward displacement of the temporal horn on the affected side and partial effacement of the vestibule when lateralized tumors reach large size.

Protrusion of a tumor into one side of the third ventricle produces unilateral deformity of the ventricular outline, varying widely in degree depending upon the size of the tumor and the extent of its protrusion into the ventricle. It may be recognized as a small, well-localized filling defect visible against a background of gas as seen in sagittal view with the occiput superior, or may be so extensive as to virtually completely collapse the ventricle, leaving but a thin crescent of transparent gas (Fig. 9).

Tumor encroachment upon the third ventricle in its posterior portion is sometimes beautifully demonstrated by comparing lateral projections. Due to the fact that complete drainage of the ventricular system is never accomplished in practice, the dependent lateral ventricle, as well as the dependent portion of the third ventricle, may always be expected to contain some residual fluid. Figure 10 demonstrates graphically the manner in which residual fluid may assist in proving whether a tumor arises on the right or the left side of the midline. These diagrammatic sketches represent the dilated third and lateral ventricles of a brain harboring a small-sized tumor lying to the left of the midline in close proximity to the posterior portion of the third ventricle.

As seen in left lateral projection (Fig. 10*A*, above), the tumor shown in solid black is seen to be clearly outlined, invading the posterior portion of the third ventricle. In right lateral projection, on the other hand (Fig. 10*B*, above), no filling defect whatever is to be seen. Two additional

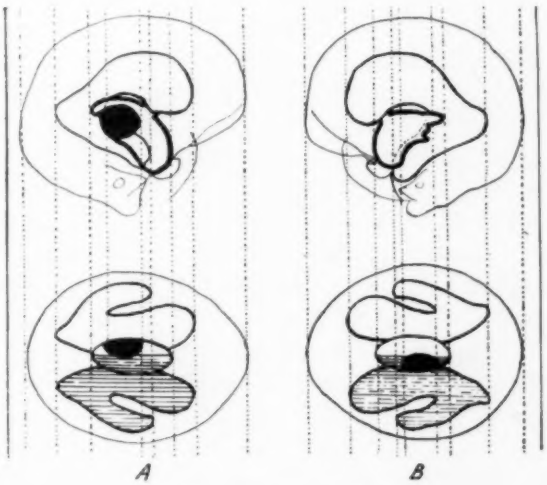


Fig. 10, *A* and *B*.

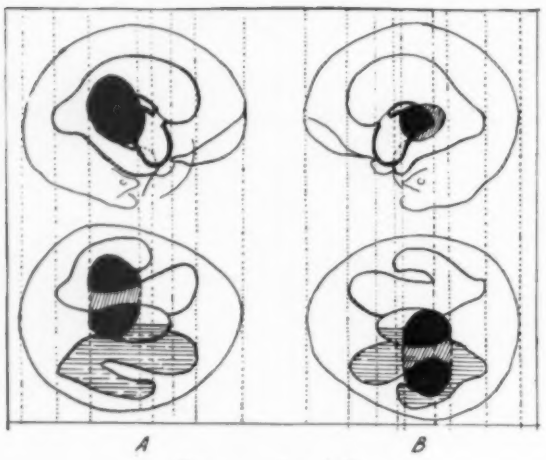


Fig. 11, *A* and *B*.

sketches showing the third and lateral ventricles as they would appear if viewed from the vertex of the skull with the patient in routine position for lateral filming (Figs. 10*A* and 10*B*, below), one finds the explanation for the striking difference shown by tumors of this sort in right and left lateral projections. Residual fluid is represented by the shading of the dependent lateral ventricle and the dependent portion of the third ventricle. When the tumor side of the brain lies uppermost, the tumor outline is clearly silhouetted against supernatant gas within the third ventricle. When the unaffected side is uppermost, the tumor is submerged in the dependent fluid collection and the observer recognizes no third ventricular filling defect. It is obvious that one can expect to encounter this diagnostic sign only when a tumor actually protrudes into the third ventricle and only when such protrusion is not sufficiently extensive to extend completely across the entire width of the ventricle.

Compression and elevation of the corpus of the lateral ventricle by underlying tumor are easily demonstrable in sagittal projection with the occiput superior, as shown in Figure 9. Again the degree of displacement and compression may be expected to vary with the size of the tumor itself. In the schematic drawings of Figure 9, the posterior horns of the lateral ventricles are not shown, whereas in ventriculograms the outlines of these gas-filled cavities may prove annoying. Careful examination of right and left lateral projections will often show valuable lateralizing signs, again by virtue of selective filling of right or left lateral ventricle made possible by residual fluid which gravitates to whichever side may be dependent. Figure 11, consisting of four sketches comparable to those reproduced in Figure 10, demonstrates the type of changes one may expect to find in the corpus of the lateral ventricle on the affected side.

Turning once more to Figure 9*B*, one can see depression and compression of the temporal horn produced by a large tumor lying to the left of the midline. In tumors of sufficient size to produce this change, deformity of gas containing ventricular structures will often enable the observer to recognize a considerable portion of the periphery of the tumor mass.

Hypothalamic tumors seen in sagittal view, occiput superior, characteristically displace the posterior portion of the third ventricle somewhat upward as well as toward the unaffected side (Fig. 12) without producing displacement or compression of the corpus of the lateral ventricle.

Case VI, an excellent example of a small thalamic tumor, is illustrated with reproductions of three original ventriculograms and three corresponding line drawings. This particular tumor was identified after

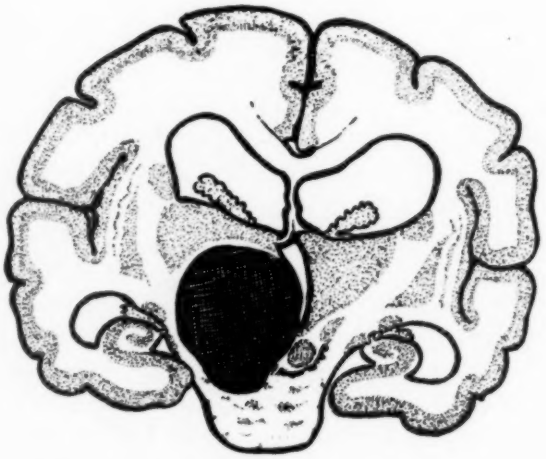
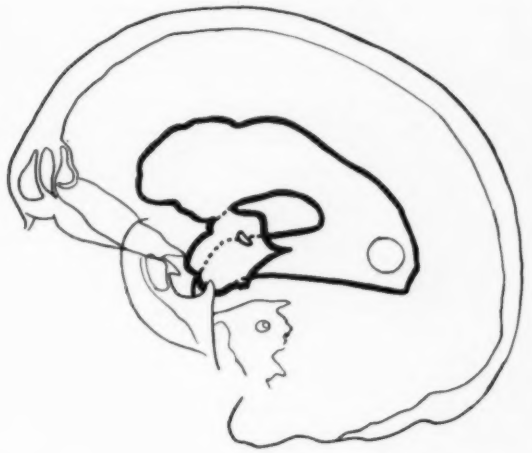
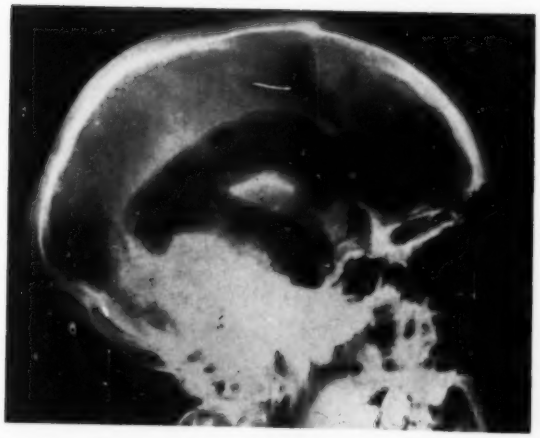


Fig. 12

A



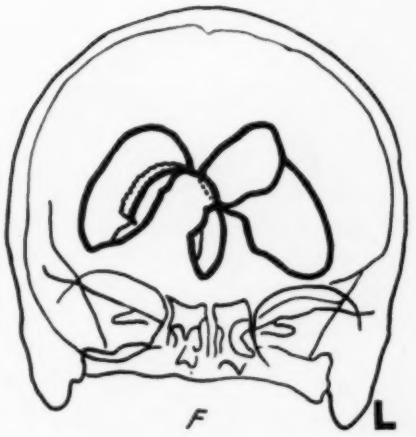
B



C

D

E



F

FIG. 13, *A*, *B*, *C*, *D*, *E* and *F*. Case VI (288180).

operation as an astrocytoma located to the right of the midline. The classical ventriculographic signs of the soft tissue filling defect involving the right side of the posterior portion of the third ventricle superiorly are clearly recognizable. The floor of the corpus of the right lateral ventricle is slightly elevated as seen in the occipital sagittal projection (Fig. 13). Asymmetrical deformity of the third ventricle is particularly striking in this case when right and left lateral projections are compared.

Case VII is reproduced in sketches based on the original ventriculograms in right and left lateral as well as in the usual sagittal projection with the occiput superior. This tumor was a large glioblastoma involving the left thalamus. It will be noted in Figures 14*A* and 14*B* that the third ventricle, as seen in lateral projection, does not differ greatly in the right and the left lateral views. The corpus of the left lateral ventricle when the left side is uppermost shows, however, a very definite encroachment upon its cavity by the soft tissue mass of the tumor itself. In fact, this defect is sufficiently large to involve the anterior portion of the vestibule and the superior margin of the temporal horn. The normal contours of these structures can be faintly seen by virtue of the fact that the tumor has not completely obliterated the entire

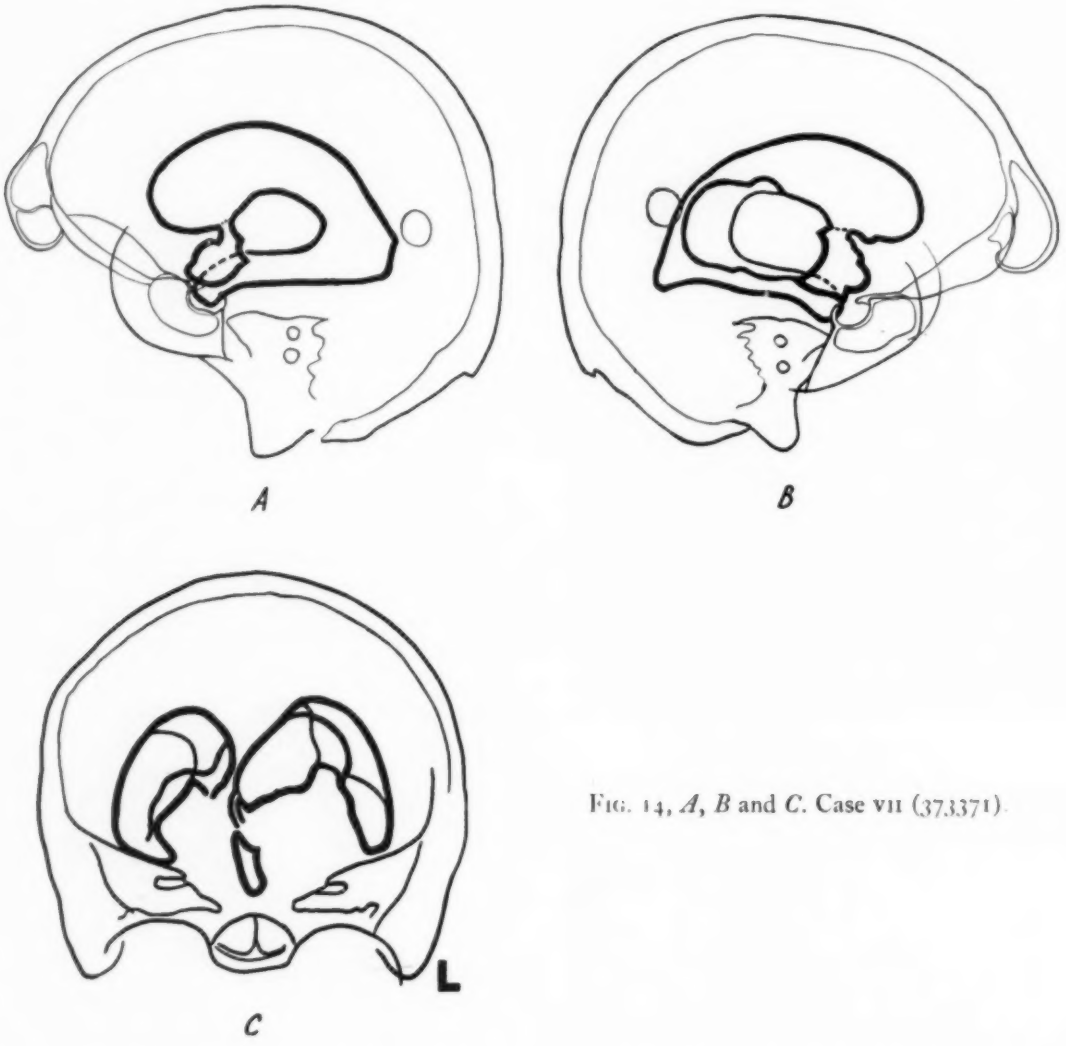
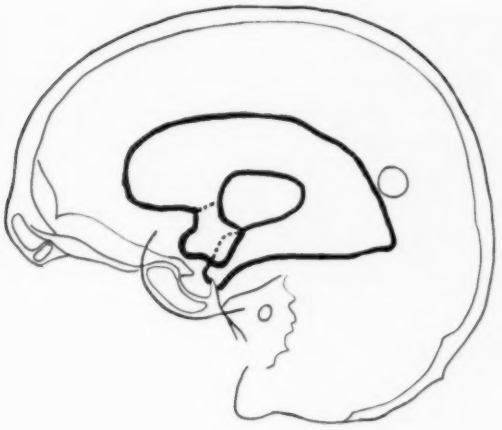


Fig. 14, *A*, *B* and *C*. Case VII (373371).

A



B

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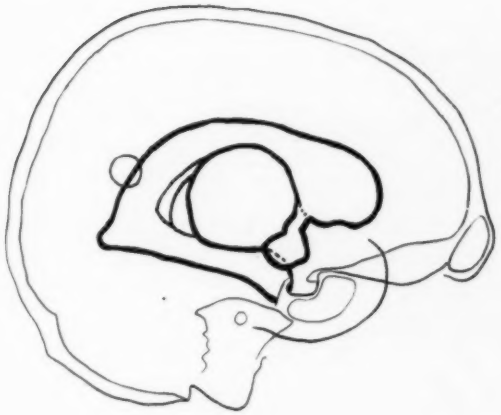
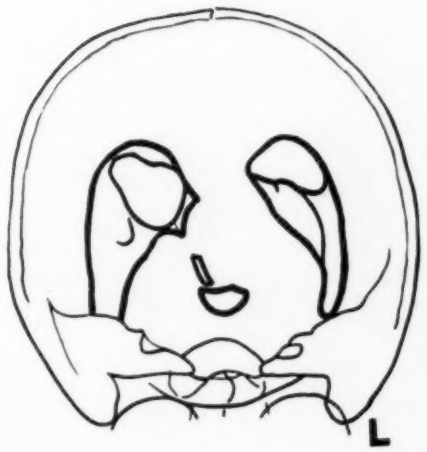


D



E

Fig. 15, *A*, *B*, *C*, *D*, and *E*. Case VIII (354901).

ventricle in these regions. The sketch representing the sagittal view (Fig. 14*C*) shows characteristic elevation of the corpus of the left lateral ventricle and definite encroachment by the tumor mass. In this view, one also sees displacement of the largely obliterated posterior portion of the third ventricle away from the tumor side. viewed in the left lateral projection; when viewed in the right lateral projection these characteristic signs are no longer to be seen. There are slight differences in the size and shape of that portion of the third ventricle which contains gas. The obliteration of the posterior portion of this ventricle is more marked in the left lateral

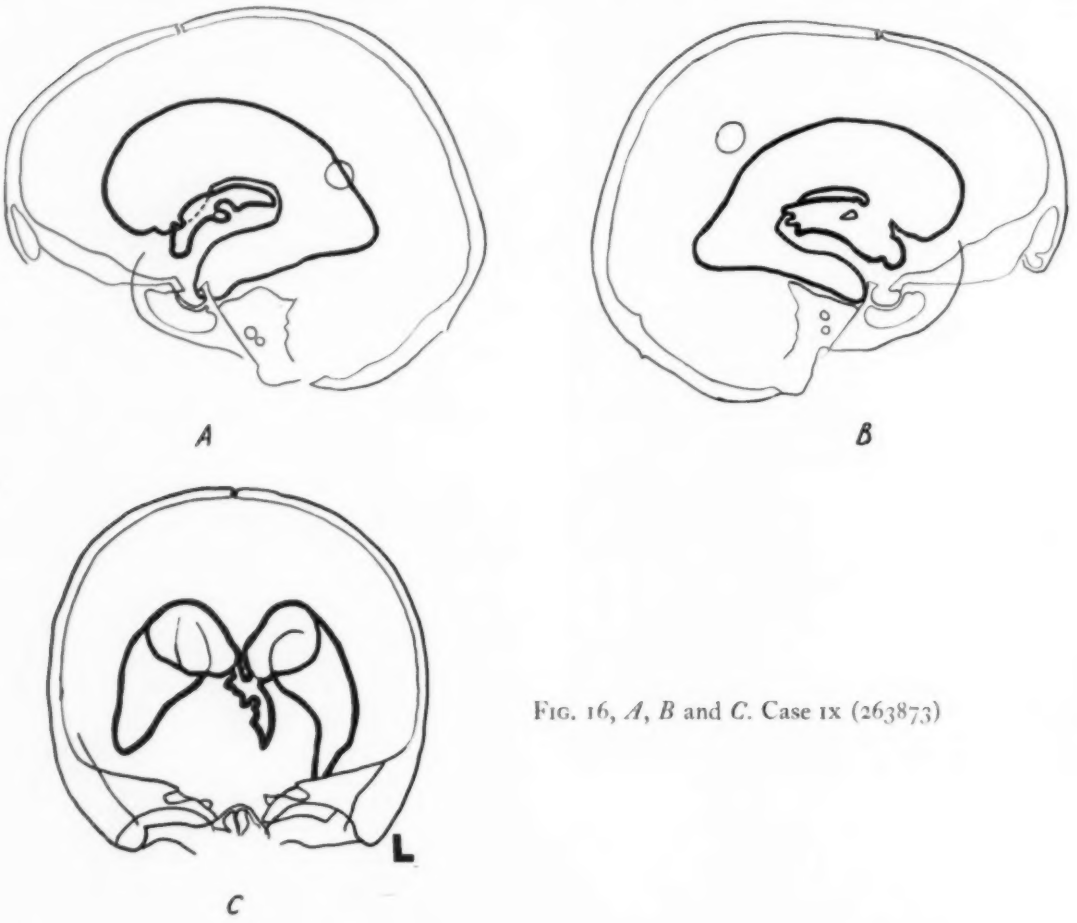


Fig. 16, *A*, *B* and *C*. Case ix (263873)

The tumor in Case viii was proved at operation to be a large sarcoma involving the left thalamus. Right and left lateral ventriculograms reproduced directly (Figs. 15*A* and 15*C*) show marked elevation of the floor of the corpus of the left lateral ventricle and partial encroachment on the superior margin of the temporal horn, with obvious increase in the distance between these two structures. Virtually surrounded by gas in the ventricular system, this tumor is directly visible in its entirety when view. Further proof of lateralization to the left of the midline is obtained in the sagittal projection with occiput superior as shown in the sagittal sketch (Fig. 15*E*) taken from the original roentgenogram. The largely obliterated posterior portion of the third ventricle is sharply displaced toward the right, the floor of the left lateral ventricle is elevated by protruding tumor tissue, and some deformity is observed on the medial margin of the corpus of the right lateral ventricle.

Case IX, a large astrocytoma invading the midbrain and hypothalamus on the right, exemplifies the ventriculographic findings which are characteristic of deep-seated tumors lying well below the floor of the third ventricle. Although tumors of this type frequently involve the upper portion of the pons, they cannot be considered as properly belonging to the pontine group. Tumors of the pons are usually considered with subtentorial lesions. Situated close to the arbitrary zone of division between supra- and infratentorial structures, tumors invading the hypothalamus and midbrain produce, in a measure, ventriculographic signs common to both. The particular tumor here pictured, in line drawings taken from right and left lateral and occiput superior sagittal ventriculograms, is too far removed from the corpora of the lateral ventricles to exert any noticeable influence on their size and shape other than the generalized hydrocephalus which all tumors produce if they obstruct the aqueduct. The lateral projections in this case show a filling defect of the third ventricle restricted to the inferior margin of this cavity. The right-sided location of the tumor is reflected in the greater degree of deformity visible in the projection obtained with the right side of the skull superior. The lateral projections in this case are particularly noteworthy, however, because of the definite upward displacement of the third ventricle as shown by the failure of the dilated temporal horn to superimpose the third ventricle. This altered relationship definitely indicates the inferior position of the tumor, and simulates the upward displacement of the third ventricle commonly produced by pontine tumor. The sagittal sketch again shows little or no direct tumor effect on the corpora of the lateral ventricle. The third ventricle is displaced upward and to the left and the margin which lies adjacent to the tumor on the right is definitely deformed.

SUMMARY

Brain tumors arising in structures closely adjacent to the posterior portion of the third ventricle commonly produce characteristic ventriculographic signs by which they may be localized with considerable accuracy and by which tumor size may be fairly well recognized. Painstaking surgical and roentgenographic technique is essential to this highly specialized form of physical diagnosis. Obstruction of the aqueduct of Sylvius, almost invariably produced by tumors of this type, is helpful to the observer by providing large open spaces, the ventricles, from which cerebrospinal fluid may be withdrawn, which when filled with gas render adjacent soft tissue structures recognizable by virtue of sharp artificial contrast. The midline or lateral position of a tumor in the region under discussion can be determined by reliable and characteristic ventriculographic features. Lateralization of a tumor is indicated by asymmetry of soft tissue landmarks; these signs are recognizable in sagittal view and in comparative right and left lateral projections.*

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* Part II of this discussion, dealing with tumors situated in the vicinity of the pons, has been submitted for publication in the American Journal of Roentgenology and Radium Therapy.

THE ROENTGEN DIAGNOSIS OF INTRA-ABDOMINAL HERNIA*

By FAY K. ALEXANDER, M.D.
PHILADELPHIA, PENNSYLVANIA

HISTORY

KUMMER,[12] in 1921, was the first to visualize an intra-abdominal hernia roentgenologically, although the anatomical description of intra-abdominal hernia dates from 1776, when Neubauer[17] reported a case. Following Neubauer's case report, subsequent descriptions occurred in the literature without great additions to the knowledge of the condition, until Treitz's[18] work in 1857. In his monograph, Trietz described the fossae about the duodenojejunal junction, traced the blood supply, the so-called "vascular arch of Treitz," pointed out the "ligament of Treitz" and attempted to explain the etiology of herniae in this region.

According to Treitz, the fossae about the junction of the duodenum and jejunum were the result of failure of fusion of the peritoneum during the third stage of the process of intestinal rotation. Treitz held that these fossae, once formed, were enlarged by intestinal peristalsis and eventually produced a hernial sac. Treves[19] explained the hernial sac as the remains of the early peritoneal reflections from the primitive duodenum, the mesoduodenum. Moynihan[16] described the fossae as being produced by a failure of union of the mesenteric root with the peritoneum covering the posterior abdominal wall, a conception similar to that elaborated by Treitz.

Regardless of the exact mode of production of the intra-abdominal fossae, most authors had a more or less unanimity of opinion as to the potentiality of these fossae to receive intestinal contents, to enlarge and to form sacs and eventually result in enormous intra-abdominal herniae.

Moynihan credits Treitz with listing the following essentials as indispensable for the formation of an intra-abdominal hernia: (1) the existence of a fossa; (2) the presence of the inferior mesenteric vein in the fold; (3) freedom of movement in the small intestine to such an extent as to permit its introduction into the hernial sac formed at the expense of the fossae.

In addition, Moynihan states that the size of the hernia depends on the laxity and extensibility of the peritoneal tissue.

Exner,[10] in an excellent review of the literature, reported on what he considered to be 40 authentic cases of right, and 150 cases of left paraduodenal hernia. There have been a few scattered cases reported in the literature since the review by Exner. These were discovered in anatomical specimens or at surgical explorations. Forlini, quoted by Exner, reported but 5 paraduodenal herniae in 25,500 autopsies. Of the authentic cases of right hernia, where the sex was given, the ratio was 5 males to 1 female.

There are, however, scattered reports in the literature which suggest an embryological basis for the formation of these herniae. Treitz, Broesike[3] and Mański[14] reported the finding of hernia in young patients, and Vogt[20] reported a hernia in a newborn. While Treitz and Moynihan believed the production of the abdominal fossae was the result of embryological developmental anomalies from failure of fusion of the mesentery of the large intes tines with the posterior parietal peritoneum, Eisler and Fischer[8] and Bender[2] believe this failure of fusion of the primitive mesentery during fetal life is the prime requisite for the large intra-abdominal herniae which later develop. Hertzler[11] is also dubious as to the likelihood of a loop of gut pushing its way into one of the abdominal fossae and subsequently forming a hernia because of the lack of any differ-

* From the Department of Radiology, Chestnut Hill Hospital, Philadelphia.

ential pressure within the abdomen to propel the gut.

Andrews[1] disapproves of the explanation of the mechanism for the production of these herniae, as given by Moynihan, and lists the following as evidence against the previous conception of their origin:

1. Differential pressure within the abdomen is lacking entirely. In other words, the pressure within the main peritoneal cavity can never rise higher than within the pouch or fossae. Any *vis a tergo* to account for the formation or growth of such a hernia is lacking entirely.
2. There are literally hundreds of similar folds and fossae in the peritoneum—and they are practically never the sites of such herniae.
3. In all but a small minority of reported cases, the degree of herniation has been total or subtotal. Seldom is there more than 15 to 20 cm. of the small intestine in its normal position.
4. Reports of cases in which a hernia was found in a newborn and in the very young.
5. The herniated viscera are never anything except small bowel. Omentum, the viscus found in 9 out of 10 herniae of other sorts, has never been reported as being in the sac.

Andrews, Dott,[6] Longacre[13] and Callander, Rusk and Nemir[4] have reported autopsy and anatomical specimens of these intra-abdominal herniae. They believe that the herniae are produced during the second stage of intestinal rotation, at which time the midgut loop of the embryo is returned to the abdominal cavity and rotated around its axis, and, during the third stage of intestinal rotation when certain portions of the intestine are fixed to the posterior abdominal wall, by fusion of their mesenteries with the posterior parietal peritoneum.

If, during these stages of rotation, the umbilical midgut loop is rotated in a reversed direction, it would be possible for the small intestine to become incarcerated in its own mesentery or by the mesentery of the large bowel. It is also well within the limits of possibility for an abnormally rotated loop of gut to invaginate a portion of the mesentery of the large bowel before the mesentery of the latter fuses with the peritoneum posteriorly.

It is appreciated that any explanation of the changes which may result from faulty embryological development is theoretical and open to question, yet these explanations are quite tenable and in keeping with the embryological facts at hand. Likewise, the explanations of the formation of herniae during intestinal rotation appear to be on a more firm basis than that which requires a loop of gut to herniate itself into a preformed pouch or fossa and enlarge this fossa by intestinal peristalsis.

I have had an opportunity of examining 5 cases of what I believe to be intra-abdominal hernia and present them in the order in which they were observed.

REPORT OF CASES

Case 1 (No. 3966). White female, married, gravida II, para. II, aged twenty-nine, examined February 14, 1935.

Chief Complaint. Inconstant and vague abdominal discomfort and pain in back which at times became severe enough to cause extreme distress. The pain was a dull dragging type of discomfort which became cramp-like and sharp during the severe attacks.

Present Illness. The patient had had this type of abdominal discomfort as long as she could remember, with the exception of the severe attacks of pain which developed after the birth of her first child. Since that time, the pain became more intense and the incidence of the attacks increased. It is of considerable interest to note that the patient volunteered the information that reclining or lying down gave considerable relief of symptoms and also that her pain became more pronounced after meals and was exaggerated particularly by walking. There was a distinct quantitative food relationship to the abdominal pain, in that the patient stated she had less discomfort if she ate more frequently and had smaller meals. There was no qualitative food history or associated sys-

Fig. 1. Case 1. Small intestine entirely in mid-abdomen. Note close approximation and distention of the coils of the jejunum and upper ileum.

temic symptoms which were relevant to the chief complaint.

Past Medical History. This was of interest because of the past studies. The patient had had a barium enema examination, lumbar spine and sacroiliac studies made nine months before the gastrointestinal series. These examinations were negative and we suggested an investigation of the upper intestinal tract. A gynecological consultation revealed some retroversion and, following the positioning of a vaginal pessary, the low back pain was relieved somewhat. The abdominal discomfort persisted, however, and the patient was referred to the department for study of the gastrointestinal tract.

Physical Examination. This was negative. Examination of the abdomen was repeated after the roentgenoscopic observation of the small intestine, but nothing of any significance could be found.

Laboratory Studies. Negative.

Roentgen examination revealed the appearance as seen in Figure 1. During the roentgenoscopic examination it was noticed, following the passage of the barium into the jejunum, that it did not occupy the usual position of the small intestine, but instead the coils were in the midline. It was not possible to distinguish any group of vertical coils nor was it possible to identify any of the more distal horizontal or oblique coils. The mucosal pattern was normal. It was impossible to separate the coils of the intestine by manual palpation; one had an impression that the intestine was contained in a sac. There was a definite delay in gastric emptying and small intestinal motility. Barium enema revealed a normal large intestine. *Summary.* In this patient there was delayed gastric emptying, a marked disturbance of the small intestinal motility and the small intestine was midline in position. The roentgenoscopic examination gave one the impression that the small intestine was incarcerated within a limiting sac, because of the inability to separate the loops manually. *Impression.* Intra-abdominal hernia.

Case II (No. 3201). White male, aged fifty-eight, examined April 18, 1935.

Chief Complaint. Dragging pain in abdomen, particularly in the lower left region. This pain

Fig. 2*a*. Case II. Abnormality of duodenojejunal junction together with all of the jejunum and upper ileum occupying an abnormal position and closely approximated on left side of abdomen.

was noticed usually after the patient had eaten or after he had been on his feet for a few hours. It was exaggerated particularly by walking, so much so that he adjusted his daily routine so as to prevent any such form of exercise. The pain appeared intermittently and was quite severe early in the morning around 4 or 5 o'clock. He could relieve it at that time by lying on his right side. He stated further that he usually could obtain relief during the day by reclining or lying down.

Present Illness. The patient had had pains of this type as long as he could remember and at no time did he obtain relief by medical care, nor were any of his physicians able to give him a satisfactory explanation. The pain did not become more frequent or severe.

Past Medical History. The patient had had two attacks of severe obstipation, the first attack twenty years ago and the second attack eight years ago. During these attacks he did not have a bowel movement for seven or eight days, with some abdominal distention. During these attacks, there was no nausea, vomiting or any appreciable increase in his abdominal discomfort. During the past five years, the patient had his lumbar and thoracic spine studied and also had urinary, biliary and complete gastrointestinal tract investigations, with no significant diagnosis being made. Further history was irrelevant. Appendectomy many years ago—nothing was reported at operation.

Physical Examination. The patient was well preserved for his age. He was a large man, over 6 feet tall, and weighed well over 200 pounds. Abdominal examination was negative. He apparently enjoyed unusual health, except for the above complaint.

Laboratory Studies. These were essentially negative.

Roentgen Examination (Figs. 2*a* and 2*b*). The stomach was of a modified orthotonic type, with a pyloric deformity which suggested extrinsic pressure. There was an abnormality of the third and fourth portions of the duodenum in that the bowel ran horizontally to the left side of the abdomen where it joined the jejunum. The barium meal revealed all of the jejunum and most of the ileum to lie to the left side of or in the midabdomen. The terminal ileum was in its normal position. The coils of the small intestine above the terminal ileum could not be separated manually to the extent which we would regard as normal, nor did a change in the patient's position affect the relationship of the small bowel from the appearance shown in the illustrations. There was considerable regurgitation and antiperistalsis of the barium during the time of roentgenoscopic observation, together with evidence of distention of that portion of the small intestine above the last few centimeters of terminal ileum. The impression was that of an intestine contained in a sac which was limiting the free movement of the bowel and confining it to one side of the abdomen. *Summary.* Deformity of pylorus due to extrinsic pressure; abnormal position of duodenum, jejunum and all but terminal ileum; normal large intestine. *Impression.* Intra-abdominal hernia.

Fig. 2*b*. Case II. Showing position of small intestine in relation to normal large bowel. Note lack of small intestinal loops in midabdomen.

Case III (No. 4188). White female, aged twenty-one, examined May 11, 1935.

Chief Complaint. Pain in right upper quadrant, dull and aching in character and constant in duration.

Present Illness. The pain had been present as long as the patient could remember and was exaggerated particularly by eating or by being on her feet. The severity of the discomfort could be controlled somewhat by eating smaller but more frequent meals, and considerable

Fig. 3*a*. Case III. Note abnormality of duodenojejunal junction and presence of proximal jejunum in right upper abdomen.

relief could be obtained by lying down after meals for an hour or so. There was no nausea nor vomiting.

Past medical history and *physical examination* were negative.

Laboratory studies were negative for routine procedures.

Roentgen Examination (Figs. 3*a*, 3*b* and 3*c*). The stomach was J-shaped, showing moderate ptosis. The duodenal cap was negative. There was a distinct abnormality of position of the second, third and fourth portions of the duodenum, the bowel running to the right side of the abdomen. The entire jejunum and all but the last of the terminal ileum appeared to be contained in a sac lying in the right lateral and midabdomen. There was considerable distention of the bowel and regurgitation of the barium during the roentgenoscopic examination. With the patient in the erect posture, numerous fluid levels could be seen. The cecum was found in the left lower quadrant and the terminal ileum entered the cecum on the right side. Barium enema examination revealed non-rotation of the ascending colon, hepatic flexure and transverse colon. *Summary*. Abnormal position of the duodenum, jejunum and ileum; non-rotation of that portion of the large intestine arising from the midgut. *Impression*. Intra-abdominal hernia.

Case IV (No. 4290). White female, aged thirty, married, gravida II, para. II, examined July 2, 1935.

Chief Complaint. Cramp-like pains in left upper abdomen.

Present Illness. The patient had had attacks of abdominal discomfort as long as she could remember. The pains varied somewhat in their severity, but always seemed to be precipitated by exertion and particularly by the washing and hanging of clothes. She also noticed an increase in the abdominal pain following meals and stated that it was particularly bad after eating foods containing much roughage. She could obtain relief in the recumbent posture.

Past Medical History. Irrelevant to the chief complaint.

Family History. This was of interest in that the patient stated that her sister had an "abnormal intestine" which was discovered at the time of operation, and that her brother was told his intestine was "reversed" when he was operated on. The family history was otherwise negative.

Physical examination was negative, except for the finding of considerable borborygmus on the left side of the abdomen.

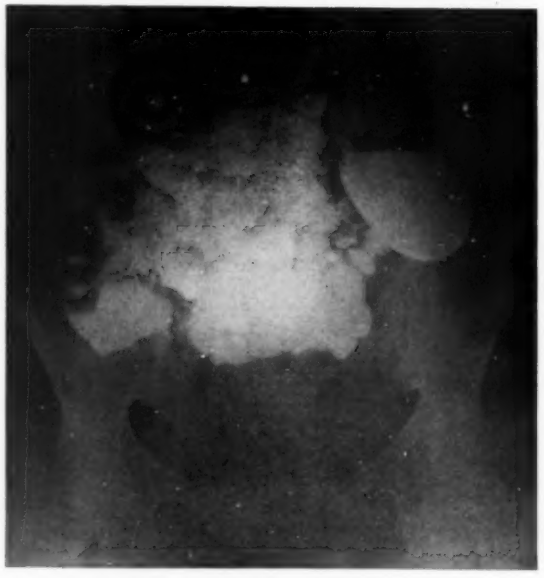

Fig. 3*b*. Case III. Jejunum and ileum on right side of abdomen; cecum in left lower quadrant with terminal ileum entering the cecum on the right side. Note presence of fluid levels and distention.

Laboratory studies were negative.

Roentgen Examination (Fig. 4). The stomach was J-shaped and in good position. During the early part of the roentgenoscopic examination, there was an intense duodenal spasm, during which time no opaque contents were expelled from the stomach. Following a period of rest, the spasm relaxed, gastric clearance became very rapid and the contents were expelled into the small intestine. All of the jejunum and the greater portion of the ileum were seen to occupy the left side of the abdomen. There was a marked restriction of motion of the coils of bowel under manual palpation and the contour of the small intestinal pattern, together with restriction of motion, simulated the findings one would expect if the bowel were enclosed in a sac within the peritoneal cavity. The mucosal pattern was normal. There was no evidence of stasis, distention or regurgitation. The lower ileum was free from the above restriction and revealed a normal pattern and normal motility on manual palpation. Changing the position of the patient did not alter the relationship of the upper small bowel within the abdomen. A barium enema examination revealed a normal position of the large intestine.

Summary. Transitory duodenal spasm; jejunum and ileum showing abnormal position.

Impression. Intra-abdominal hernia.

Fig. 3c. Case III. Jejunum and ileum on right side of abdomen; cecum in left lower quadrant with terminal ileum entering the cecum on the right side. Note presence of fluid levels and distention.

Fig. 4. Case IV. All of the jejunum and proximal ileum restricted by confining membranes to left side of abdomen. Normal appearance of terminal ileum.

Case V (No. 4506). White male, aged forty-six, examined July 8, 1936.

Chief Complaint. Inconstant midabdominal pain which at times was accompanied by nausea and vomiting.

Present Illness. This pain had been a presenting symptom for several years. It would be quite severe at times and again would be dull and aching in character. During the severe attacks nausea and vomiting might occur, which would give some sense of relief. The pain was exaggerated by hard muscular work and by eating. There was very definite relief in the recumbent posture with the thighs flexed. The patient also obtained relief following the taking of a saline cathartic, although he stated his discomfort was worse for the first thirty to forty-five minutes after its administration.

Past Medical History. This was of interest in that the patient had had numerous admissions to hospitals because of the more severe attacks of pain and, during these admissions, the clinical diagnosis varied from acute cholecystitis, duodenal ulcer and acute pancreatitis, to ureteral calculus and coronary disease. Numerous studies were made, including a gastrointestinal series, with essentially negative reports.

Family history and *laboratory studies* were negative as to the chief complaint.

Physical examination was negative on last admission, except for pain on pressure over left abdomen and very active, high-pitched, "tinny" peristalsis.

Roentgen examination (Fig. 5) revealed a J-shaped type of stomach in good position. The duodenal cap was negative. The third and fourth portions of the duodenum did not occupy the usual position and the duodenojejunal junction was well below the stomach in the midline, instead of behind it and to the left. At the junction there was noticed a dilatation of the intestine accompanied by considerable regurgitation and antiperistalsis and, immediately distal to the dilated loop of gut, a small constricted area of the bowel was seen. Distal to this constriction, the jejunum and ileum occupied the left side of the abdomen and there was marked restriction of motility of the bowel on manual palpation. The mucosal pattern was normal. The contour and configuration of the small intestine gave the impression that it was contained in a sac. There was no delay in gastric emptying or in the intestinal motility, although we could demonstrate fluid levels in the erect posture. The large bowel was negative and occupied its usual position. *Summary*. Anomalous position of the duodenum, jejunum and upper ileum. *Impression*. Intra-abdominal hernia.

Fig. 5. Case v. Abnormal relationship of duodenojejunal junction. The majority of small intestine occupies the left side of the abdomen. Note distention of the loop of small bowel proximal to its entrance into the hernia.

TERMINOLOGY

In the literature, the intestinal abnormality which we are describing has been called duodenal hernia, paraduodenal hernia (right and left), hernia into the descending mesocolon, hernia into the ascending mesocolon, mesentericoparietal hernia, etc. From the roentgen standpoint I am of the opinion that the "duodenal" portion of the title is in error, for the hernial sac does not contain duodenum, but contains jejunum and ileum. It also seems that the embryological explanation of this anomaly is not proved beyond a reasonable doubt and that the terms, "hernia into the ascending mesocolon," in the event of a right-sided hernia, or "hernia into the descending mesocolon," in the case of a left-sided hernia, are not entirely justified. It cannot be diagnosed roentgenologically. "Mesentericoparietal" is the best term to be found in the literature at the present time and, perhaps, is entirely adequate. I feel, however, that the term, "intra-abdominal hernia," is preferable, because of its simplicity and because of the antomical and pathological significance attached to it. Furthermore, one is justified in making such a roentgenologic diagnosis.

OCCURRENCE

It would seem that intra-abdominal hernia is an uncommon condition, but I do not believe the lesion is as rare as one would deduce from the comparatively few cases reported in the literature. From my experience I am convinced that the condition is being missed repeatedly during the routine gastrointestinal series which are being studied each day. These condi-

tions are not diagnosed because the progress of the opaque meal through the small intestine is not observed as carefully and as long as it should be, and the observer is often not familiar with the roentgen appearance of the normal small intestinal pattern.

CLINICAL CONSIDERATION

The clinical diagnosis of intra-abdominal hernia is a very difficult one to make, if one is to judge from the statements mentioned in the literature. Eusterman and Balfour[9] state that a diagnosis of right paraduodenal hernia has not been made before operation or autopsy at the Mayo Clinic, and there are numerous statements in the literature prior to this one to the effect that the roentgen examination is of no avail in the diagnosis of intra-abdominal hernia.[5,7,15]

It is true, the symptomatology as presented by the cases in this series was rather vague and indefinite, as far as pointing towards the investigation of any particular tract was concerned, and in my first case I was of the opinion that the lower back pain which was exaggerated by walking was lumbosacral or sacroiliac in origin and made a roentgen study of this region. I did not connect the lower back pain with the abdominal discomfort, nor could I attach any significance to the statement of relief from discomfort in the reclining or recumbent posture. At the time the gastrointestinal series was begun, I did consider the possibility of a generalized visceroptosis as an explanation of the relief from pain in the recumbent posture.

In Case II, the significant point in the clinical history was described by the patient in the following words: "dragging pain in abdomen after eating, standing or walking for any length of time." This patient was a very intelligent business man who had spent a great deal of time and money in an attempt to obtain relief from his abdominal discomfort and he stated that he obtained more relief by lying down than from all the medicines given to him by his various physicians.

With the experience of the first two cases and the results found on roentgen examination, I was interested to check roentgenologically the significant facts elicited by questioning Case III; viz., dull and aching pain in the right upper quadrant, exaggerated by eating or by being on the feet, and the lessening of this discomfort by eating smaller but more frequent meals and by lying down after meals.

Case IV presented attacks of abdominal discomfort which were precipitated by exertion and exaggerated by eating, particularly foods containing roughage. In Case V, the symptoms were very similar, with the exception that this patient obtained relief following a cathartic, although, during the first hour after taking the cathartic, his pain was much worse.

It would seem, therefore, from a study of the symptoms as obtained from the above patients, the following points should be given careful consideration in questioning a patient with abdominal symptoms which do not fit any particular symptom-complex: (1) abdominal pain which is exaggerated by exertion, by being in the erect posture, or by eating; (2) abdominal pain which is relieved by reclining or by lying in recumbent posture and which, if exaggerated by eating, is relieved by eating smaller but more frequent meals, or by eating food containing a small percentage of roughage.

ROENTGEN CONSIDERATION

The roentgen diagnosis of intra-abdominal hernia is made primarily by roentgenoscopic observation at short intervals of the barium meal as it passes through the small intestine. The usual roentgen examination of the stomach and duodenal cap will not enable one to diagnose this condition, or to justify the statement as to its absence. My procedure in all routine gastrointestinal cases is to follow the progress of the meal through at least the proximal half of the jejunum, and such a

routine renders it possible to diagnose or exclude intra-abdominal hernia.

In the patients in which a diagnosis was made, the distal duodenum and duodenojejunal junction were situated abnormally to the extent that the opaque meal did not follow the usual anatomical course. It is not believed, however, that a variation in the anatomical course of the duodenum

Fig. 6. Case vi. Small intestine entirely in midline. Close approximation of the loops of small bowel held together by adhesions and simulating a hernia.

and duodenojejunal junction is in itself necessarily an indication of intra-abdominal hernia, but in that this observation was found in every instance reported above, it should warn one of such a possibility.

The small intestine may occupy the right side, midportion or left side of the abdomen. The coils of intestine are grouped very closely. The mucosal pattern has been normal in my experience. There may be considerable churning, regurgitation and even distention of the small intestine, with the presence of fluid levels and, as in Case v, one may be able to demonstrate where the small intestine enters the hernia.

The loops of bowel present an appearance and configuration as though they are contained in a sac or confining boundary, rather than being allowed the freedom of the abdomen justified by the length of the small intestinal mesentery. There is little movement on manual palpation and a change in position or posture of the patient produces little, if any, change in the relation of small intestine to the abdominal cavity. Manual pressure on one area of the mass of gut is transmitted throughout the mass in a manner similar to the transmitted fluid waves in ascites. The distal ileum has been found free of the sac in my experience and can be demonstrated entering the cecum.

DIFFERENTIAL DIAGNOSIS

Postoperative Adhesions. This condition will, at times, cause an appearance of the small intestine which simulates very closely the appearance seen in an intra-abdominal hernia. I have one case in my files which demonstrates this parallel very nicely (Fig. 6).

This patient was first examined in January, 1931, at which time the upper intestinal tract was found to be negative, but a carcinoma of the ascending colon was found. This was removed in two stages and an ileocolic anastomosis was done. Roentgen examination in June, 1933, revealed an appearance on the films which could not be differentiated from intra-abdominal hernia, without the history of previous operative interference.

Peritonitis. It is possible to conceive that a suppurative peritonitis from a ruptured viscus, or as a result of tuberculosis, could result in the formation of adhesions to the extent that an appearance would be produced similar to that shown in the present series of cases. This type of condition has not come under my observation, although the diagnosis could be made easily from the clinical history.

Intestinal Non-rotation. I see no reason for confusion in the differential diagnosis between intra-abdominal hernia and intestinal non-rotation, for in the latter condition, uncomplicated, the cecum is reversed and the ileum enters the large bowel from the right.

Congenitally Short Mesentery. The possibility of a congenitally short mesentery being mistaken for an intra-abdominal hernia is likely, and I do not believe that if the mesenteric root is in its normal position, viz., running from the upper left abdomen to the lower right abdomen, it is possible to differentiate this from a centrally placed hernia.

SUMMARY

Five patients with intra-abdominal hernia are reported. Some of the pertinent literature is referred to and its relationship to the roentgen diagnosis is considered.

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ROENTGEN THERAPY OF CHRONIC SINUSITIS IN CHILDREN*

By R. RHETT RATHBONE, M.D.
Children's Hospital; Garfield Hospital; Warwick Memorial Clinic
WASHINGTON, D.C.

SINUSITIS in childhood is a very common disease. Its frequency of recognition is dependent upon the alertness of the pediatrician or roentgenologist, as its symptoms are often slight or masked entirely by its sequelae. If its serious complications are to be prevented, early recognition and treatment are essential.

DIAGNOSIS

The diagnosis of chronic sinus disease is not easy. In infants, syphilitic rhinitis with snuffles and diphtheritic rhinitis must be excluded. In children, allergic rhinitis and sinusitis must be ruled out. In children, the frank cases of sinus disease are easily recognized; in many, however, the sinusitis is often masked or overshadowed entirely by a severe and chronic cough. Many children are sent to the roentgenologist with a possible diagnosis of tuberculosis because of malnutrition and a chronic cough. The diagnosis is usually chronic sinusitis and the roentgenogram of the chest is characteristic, showing an increased prominence of the trunk shadows extending out from the hilus, especially toward the base, and a general thickening at the roots of the lung. Many cases of previously unsuspected sinus disease have been picked up by noting these pulmonary changes, as stressed by Manges,[10] Wasson and Waltz,[13] and suggesting that the sinuses be investigated. It is essential that this be done, as Clerf[3] considers sinus disease the most important cause of bilateral bronchiectasis (82.4 per cent) and believes it is often overlooked because of the lack of symptoms referable to the sinuses. In this small group we have encountered 2 cases of bilateral bronchiectasis, in patients aged six and eight. Both cases give a history of running nose and frequent colds followed by a cough since infancy. They have a purulent sinusitis that has been refractory to both surgical and roentgen treatment. The pus in the sinus drains into the lungs and the pus in the bronchi is coughed and sneezed into the sinuses, forming a vicious circle that is difficult to treat. Davis[6] believes that lobectomy in selected cases, as well as active treatment to the sinuses, is the only method of curing these advanced cases. It is our aim to diagnose and treat these diseased sinuses in infancy and childhood to avoid this serious complication.

Sinus disease is frequently associated with an otitis media or mastoiditis in infants (Cullom,[4] Fowler,[7] Manges[11]) and is generally overlooked, the attention and treatment being directed toward the ears. Campbell[2] found that practically all of 150 consecutive patients with ear infections had sinus disease, which he looked upon as an etiologic factor in the production of the otitis. Children and infants with repeated attacks of otitis should have the sinuses investigated, as we have been able to abruptly terminate these attacks by treating an unrecognized sinus disease. Knowing the frequency of repeated otitis and mastoiditis in some children I cannot overemphasize this point.

Asthmatic bronchitis in children is often due to sinus disease. Lierle[9] reports 20 cases of asthma in children, in all of whom there was sinus disease, and Manges reports sinus disease in 60 per cent of 354 asthma cases. Simple cervical adenitis usually follows a tonsillitis, but some cases are secondary to sinus disease. When cervical adenopathy does not respond promptly to

* From the Radiological Clinic of Drs. Groover, Christie and Merritt, Washington, D.C.

therapy, sinusitis must be considered as a possibility, as several cases refractory to, or recurrent after, local roentgen therapy have cleared up promptly after the sinus disease was recognized and treated. Three cases of pronounced retropharyngeal swelling in infants with symptoms of enlarged thymus were also associated with sinus disease.

In the roentgen examination of children for sinus disease, it is essential that an absolutely true lateral film be taken of the skull to show the nasopharynx for adenoids, as well as the usual posteroanterior views. The roentgen examination in infants and children is not complete without a statement as to the size of the adenoids, as enlarged adenoids will give a clinical picture identical to chronic sinus disease. We are convinced that enlarged adenoids are also the cause of many cases of sinus disease. Adenoidectomy is usually considered a very simple procedure; however, we have noted that they are often incompletely removed at operation and not infrequently there is no improvement in the children until the adenoids are completely removed at a second operation.

TYPES OF CASES SUITABLE FOR ROENTGEN THERAPY

Roentgen therapy is not a panacea for sinus disease; however, in selected cases the results have been very good. It is a simple, safe method that can be used in infants as well as children, and we believe that if infants can avoid a chronic sinus disease much of the later sinus disease, otitis media, mastoiditis, cervical adenitis and asthma may be avoided.

We do not, as a rule, treat acute sinus disease with roentgen therapy. The acute cases generally recover with simple medical treatment. We do not recommend treatment in cases with frank pus in the nose unless the roentgen and clinical examination shows a diffuse lymphoid hyperplasia throughout the nose and throat. We believe purulent cases without lymphoid hyperplasia are best treated by the oto-laryngologist, as most of our failures have been in this group.

The ideal type of case for roentgen therapy is the child with a diffuse lymphoid hyperplasia throughout the nose and throat with a watery or mucous nasal discharge, a history of frequent colds, a chronic cough, and where the roentgenogram demonstrates hyperplasia of the mucosa of the antra or ethmoids. Such cases are always helped by roentgen therapy as shown both clinically and roentgenologically, and the benefit is usually a permanent one. After roentgen therapy the children will have fewer colds, and the sinuses rarely become involved. If involved, they clear up in a few days without any special therapy. Case 1 is an example of this type of disease.

Another group of patients deserve special mention. These are the infants or children who have frequent colds, and with every cold develop either an otitis media or cervical adenopathy. Such infants invariably have a diffuse lymphoid hyperplasia throughout the nose and throat with large adenoids. Most otolaryngologists hesitate to do a tonsillectomy and adenoidectomy on infants under three years of age. When it is done, the attacks of cervical adenopathy are usually stopped; however, it frequently has no effect on the repeated otitis. This is due to the horizontal position of the eustachian tubes and to the lymphoid hyperplasia about the orifice of the tubes. Adenoidectomy sometimes helps, but frequently does not, as it is impossible to surgically remove the lymphoid tissue around the orifice of the eustachian tubes. It has long been an established fact that this lymphoid tissue yields readily to small doses of roentgen therapy. In infants with a history of frequent otitis we recommend a roentgen examination of the sinuses and, if they are involved, or if the infant shows a lymphoid hyperplasia throughout the pharynx, we recommend roentgen therapy during either the acute or chronic stage of otitis media. One infant, aged sixteen months,

with a purulent pansinusitis had, in two months preceeding the roentgen therapy, fourteen myringotomies and during this time either one or both ears were draining continuously. Following the first treatment the child improved, the ears were dry in two weeks, and for the past year, since therapy, the child has had only occasional colds, no sinusitis and no otitis. Crain and Sloan[5] have also reported the great value of roentgen therapy in otitis and mastoiditis in infants. With roentgen therapy many such infants can be carried along until they are old enough to have a tonsillectomy and adenoidectomy done. Roentgen therapy will never supplant this operation, and in older children we always advise it, after the sinus disease has subsided if the tonsils and adenoids are enlarged or infected. Following roentgen therapy to the sinuses, the adenoids usually regress 25 to 30 per cent. We do not think a tonsillectomy and adenoidectomy should be done in the presence of sinusitis but after roentgen therapy, as these are the children that are often worse after operation.

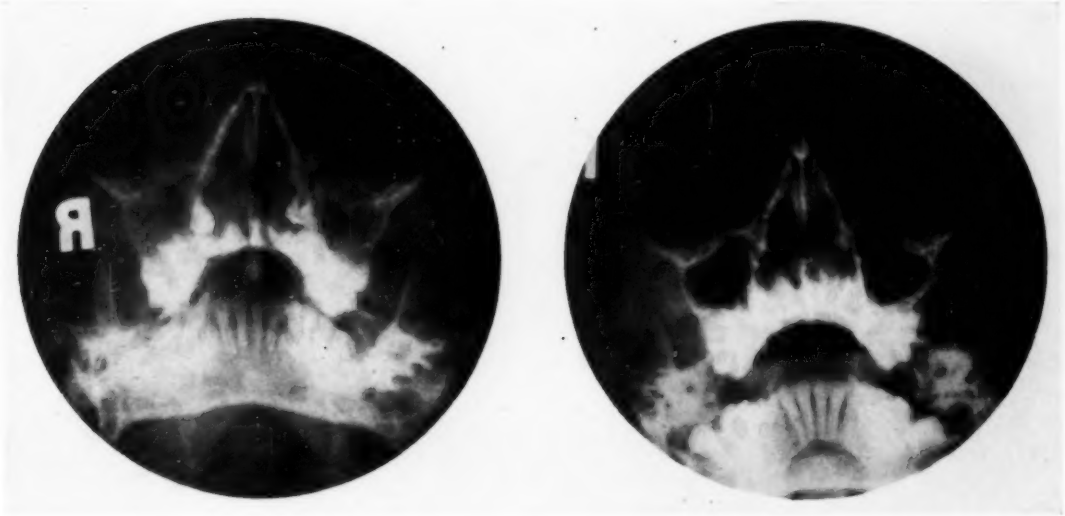
The treatment of asthma in children is often difficult. We have had excellent results in 6 cases of so-called asthmatic bronchitis in nonallergic children that was due apparently to chronic sinus disease. These children had frequent colds, and with the cold usually developed asthma, often severe. Following roentgen therapy the sinusitis and asthmatic attacks entirely disappeared in 4 of these cases. The other 2 children still had attacks of sinus disease and asthma, but were definitely improved, as the asthma was less severe and less frequent. In 5 allergic children with asthma and sinusitis, none were cured following roentgen therapy, 2 were improved and 3 showed no change.

TECHNIQUE

The use of roentgen rays in the treatment of sinusitis is not new. In 1923, Osmond[12] reported marked improvement in 12 cases after small doses of roentgen rays. In 1934, Butler and Woolley[1] reported good results in 700 cases of sinus disease.

In our experience the quality of the radiation used is of no significance, provided some filtration is used. At Children's Hospital we use 125 kv. (peak), 5 ma., 12 inch distance, 5 mm. aluminum filter and a dose of 120 r (measured in air). At Garfield Hospital we use 220 kv. (peak), 20 ma., 50 cm. distance, 0.5 mm. copper filter and a dose of 100 r (measured in air). Depending on the size of the child, three overlapping areas 10 × 10 cm. or 7 × 7 cm. are treated: one anterior, and a right and left lateral. The eyes and eyebrows are protected with 1 mm. lead shields, oval in shape, of various sizes to fit the bony orbits. A small band of adhesive tape across the nose holds the shields in place. The eyebrows are protected as the frontal sinuses are not developed in infants and are rarely involved in children. The anterior area extends from slightly below the hairline down to the upper lip; the lateral areas extend from the mastoid process to the forehead and nose, so that the ear and eustachian tube are treated. A total of six treatments is our usual routine. The treatments are given three times a week, over a two-week period, treating only one area per day in rotation with 100 r or 120 r (measured in air), depending on the available equipment. This dose may produce a temporary partial epilation over the temples but never epilates the protected eyebrows. In children with a severe cough the chest is treated once or twice, giving 100 r at the conclusion of the sinus treatment. In treating the sinuses larger doses in a shorter time have been tried, but because of the frequent severe headache produced the smaller dose without this difficulty is routine. In 7 cases with recurrent sinus disease the series has been repeated at the end of six months to a year with excellent results in 4 of them.

We are frequently asked about the dangers of treating sinuses with roentgen therapy. Because of the very small dose advocated the treatment is absolutely harmless, and without any immediate or



a *b*

Fig. Case 1. Before, *a*, and after, *b*, roentgen therapy. Chronic cough and malnutrition of one year duration. Thought to have tuberculosis before sinus disease was discovered. Has been perfectly well three and a half years since treatment.

late ill effect. The dose is comparable with the exposures necessary twenty-five years ago for the routine roentgen examination of the sinuses, using gas tubes and no intensifying screens, and countless thousands of such examinations have been made. Since 1919 my senior associate, Dr. E. A. Merritt, has also used approximately twice this dose for complete epilation of the scalp for ringworm in infants and children, treating over 4,000 cases without evidence of injury. Butler and Woolley,[1] and also Heine,[8] report experimental work in which there was microscopic evidence that small doses of roentgen radiation did not injure the cilia.

The average age of the children studied in this group was five years, the youngest

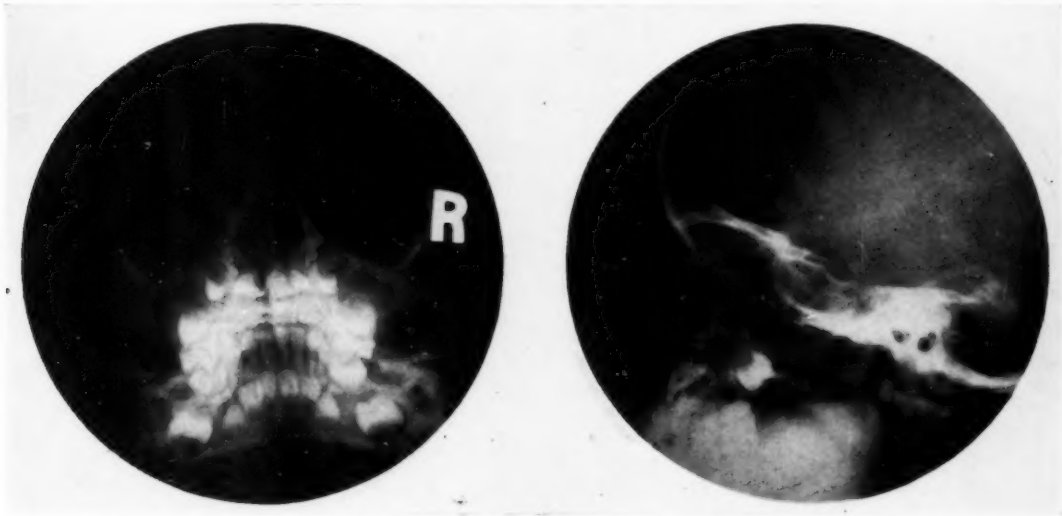


Fig. 2. Case 11. Before roentgen therapy. Chronic cough and severe asthma of two months' duration. Note enlarged adenoids.

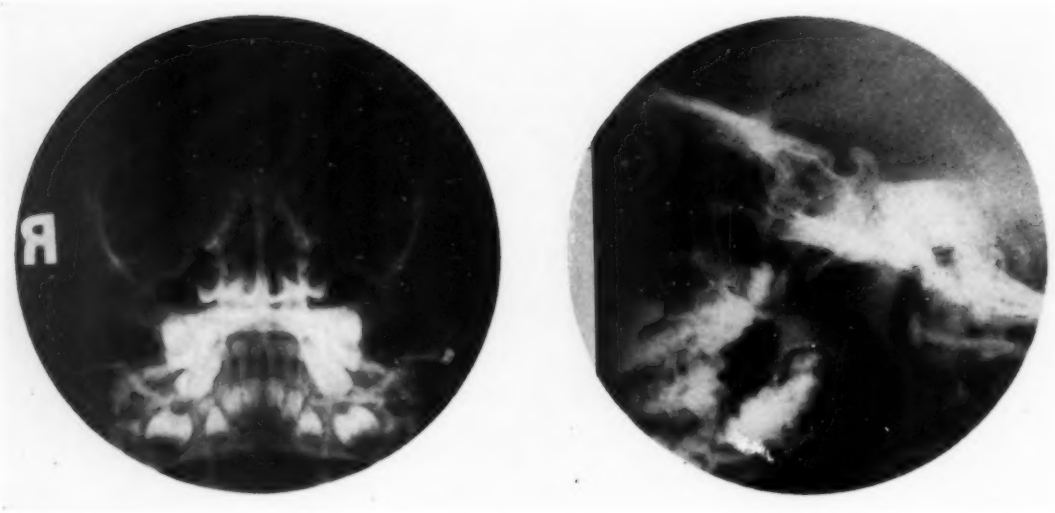


Fig. 3. Case II. Sinuses normal after roentgen therapy. Adenoids have regressed 25 per cent. Patient entirely well for eighteen months, then had recurrence of sinus disease without asthma. Is receiving second series of roentgen therapy at present time.

being three months and the oldest twelve years, which is the age limit at Children's Hospital.

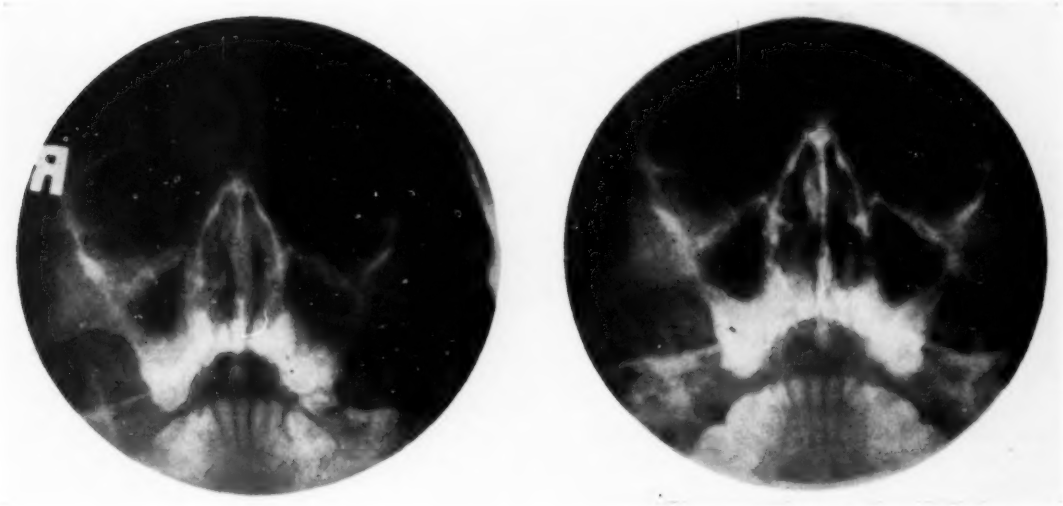
During the past three and a half years, 124 children have been treated for sinus disease. Many of these were dispensary or clinic patients and follow-up has been difficult or impossible. We have included in this report only those cases which have had at least one check-up roentgen examination after treatment. Most of these cases have had a roentgen examination after treatment and then one every six months, to check the permanency of the results. All reported cases have been followed clinically by us or the referring physician at least one year after treatment.

Cases reported as cured, improved immediately after treatment, and have been symptom-free one to three and a half years since treatment, and the check-up roentgen examinations showed the sinuses to be entirely normal. Cases reported as improved are those in which the local symptoms and sequelae were greatly or entirely relieved but the check-up roentgen examination showed some degree of sinus disease to be still present. Cases reported as not improved had little or only temporary improvement in symptoms and the roentgen examination showed definite sinus disease to be present. Seventy cases have been followed as outlined and 40, or 57 per cent, were cured; 20, or 28 per cent, improved and 10, or 15 per cent, not improved.

REPORT OF CASES

Case I. H. S. The patient, a white female, aged eight, was first seen in October, 1933. During the preceding winter the patient had an almost continuous cold and a persistent cough which kept her out of school more than half of the year. She was under the care of three different physicians with local treatments to nose, and cough medicines, without relief, and it was decided that a bilateral radical antrum operation was necessary. During the summer the patient was fairly well. With the first cold weather in September, 1933, the severe cough and nasal discharge returned. Roentgen examination of sinuses showed marked hyperplasia of the mucosa of both antra (Fig. 1*a*). Roentgen therapy was advised and given. Since treatment the child has not missed a day of school because of colds or coughs. Five subsequent roentgen examinations in three and a half years have shown the sinuses to be normal (Fig. 1*b*).

Case II. J. W., colored male, aged three, was first seen in June, 1935. For two months the patient had had a cold, a running nose and headache. Soon after the onset of the cold a cough



a *b*

Fig. 4. Case III. Before, *a*, and after, *b*, roentgen therapy. Frequent colds and chronic cough of three years' duration. Two attacks of otitis media and one attack of cervical adenitis. This hyperplastic type of sinus disease always responds to roentgen therapy. Has been perfectly well for three years following treatment.

developed, followed by attacks of asthma. During the second month the asthmatic attacks were severe and the patient lost 4 pounds in weight. There was no history of allergy. Roentgen examination of the sinuses showed complete opacity of the ethmoids and antra, and marked enlargement of the adenoids (Fig. 2). Roentgen therapy was advised and given; at its conclusion the asthmatic attacks and headaches had stopped. The roentgen examination of the sinuses two months after treatment showed them to be entirely clear and the adenoids to have regressed slightly (Fig. 3). The child remained perfectly well for eighteen months when he returned with another cold, of one month duration and without asthma. The roentgen examination showed both antra to be opaque and the adenoids still enlarged. A second series of roentgen irradiation is now being given, to be followed by adenoidectomy, the omission of which was probably a factor in the recurrent sinus disease.

Case III. R. S., white male, aged eleven, was first seen in September, 1934. The three previous winters the child had frequent colds followed by a severe, persistent cough which always lasted several months. The child was apparently well during the summer months. During the winter of 1933 there were two attacks of otitis media requiring myringotomy, and one attack of cervical adenitis. In September, 1934, the child contracted a cold followed by a severe cough. For three weeks the mother was up several times each night because of this cough. The child was 4 pounds underweight and was thought to have tuberculosis. Roentgen examination of the chest showed no evidence of tuberculosis, but showed increased trunk markings and prominent dense hila, suggestive of sinus disease. Roentgen examination of the sinuses was recommended; the examination showed hyperplasia of the mucosa of both antra (Fig. 4*a*). Roentgen therapy was advised and given. At the conclusion of treatment the child had stopped coughing and the mother was delighted. Four months after treatment the sinuses were entirely clear (Fig. 4*b*), the child's weight was normal and he was going to school regularly. For the past three years the child has been well, having only an occasional cold. Three subsequent roentgen examinations of the sinuses have shown them to be clear.

SUMMARY

Sinus disease in children is usually masked by complications such as severe cough, otitis media, cervical adenitis or asthma.

Seventy children with sinus disease have been followed from one to three and a

half years with roentgen examinations before and after roentgen treatment. In this group 57 per cent were cured, 28 per cent were improved, and 15 per cent were not benefited by the treatment.

A high percentage of cures may be expected if only the recommended types of sinus disease are treated by roentgen therapy.

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Vol. 38, No. 1

OSTEITIS DEFORMANS (PAGET'S DISEASE)

FISSURE FRACTURES—THEIR ETIOLOGY AND CLINICAL SIGNIFICANCE*

By M. LOWRY ALLEN, M.D., *and* RUTHERFORD L. JOHN, M.D.,
PHILADELPHIA, PENNSYLVANIA

IN 1876 Sir James Paget described the osseous dystrophy which since then has borne his name—Paget's disease. His classic description said:[6] "The bones enlarge and soften and those bearing weight become unnaturally curved and misshapened." With the advent of the roentgen ray, new knowledge has been acquired as to the skeletal changes produced by this disease, while numerous pathologic studies have revealed many of the finer microscopic alterations produced in the bone architecture. The modern concept of the disease has been well summarized by Traver[9] as follows:

> The pathology of Paget's disease consists in the enlargement of one or more bones with replacement of normal bone by bone of a spongy structure. The bone marrow later becomes fibrous and new bone is formed in the marrow spaces. There is first softening and then overgrowth of bone. In the long bones there is an increase in the width and length. During the early stages the bones are soft and cut easily with a knife. It is at this stage that deformities occur. Later there is a thick deposit of subperiosteal bone and the surface of the bone becomes rough and irregular. In radiographs there is seen thickening of the cortex with enlargement and bowing of the long bones, and a rearrangement of the trabeculae or bundles running longitudinally. The new cortical bone may show multiple longitudinal cystic-like areas. The medulla also shows mottled areas of rarefaction which extend into the epiphyses.

A few modern writers have called attention to the occurrence of fissure fractures on the convex surface of the curved long bones in cases of marked Paget's disease. These are manifested roentgenologically by one or usually more fissure-like, transverse lines of rarefaction on the convex surface of the affected bone. Gutman and Kasabach[2] say that "marked bowing of the long bones may lead to the development of numerous incomplete fissure fractures on their convex aspect. Pathologic fractures, characteristically transverse, usually follow." Traver says that "incomplete fissure fractures are common and with slight trauma may become complete fractures." Despite these clear-cut statements there is some confusion in the literature as to the nature and etiology of these fissure fractures and the proper terminology to be applied to them. Brailsford,[1] quoting Looser,[4] does not believe them to be true fractures, but refers to them as pseudo-fractures. He bases his belief on Looser's work which endeavors to show that these translucent lines seen in the roentgenograms are simply zones of metaplasia; the so-called "Umbauzonen" or Looser's zones of metaplasia. These lines or zones, he believes, occur not only in osteitis deformans but also in osteomalacia, late rickets, osteitis fibrosa cystica, and osteogenesis imperfecta. Schmorl,[8] however, after microscopic studies of bone obtained at necropsy from cases of Paget's disease, believes that these rarefied zones in Paget's disease represent an entirely different process from the similar phenomena occurring in osteomalacia, late rickets, osteogenesis imperfecta and osteitis fibrosa cystica. In his studies of the so-called metaplastic zones in osteitis deformans, he found an entirely different picture from that prevailing in the other named conditions, although roentgenologically they resemble one another. In Paget's disease these zones were filled with new-formed osseous tissue exhibiting the mosaic structure characteristic of Paget's disease. From this he concludes that these

* From the Departments of Roentgenology and Orthopedic Surgery of the Hospital of the Protestant Episcopal Church, Philadelphia.

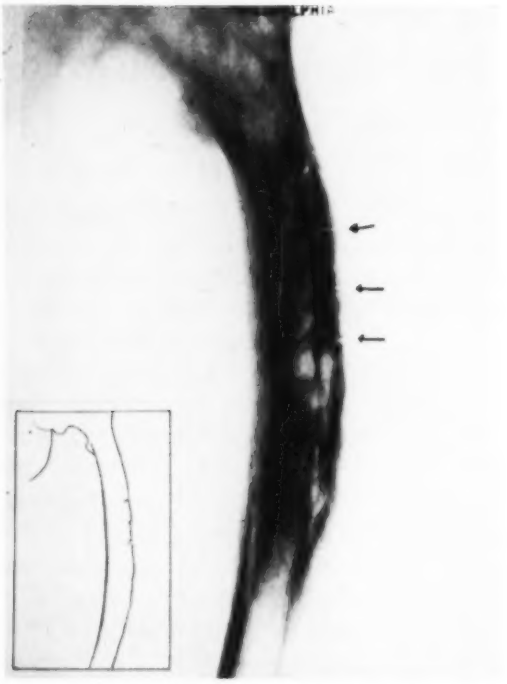

FIG. 1. Case 1. There is marked bowing and enlargement of the left femur, with thickening of the cortex. Note the three translucent lines on the convex surface representing three incomplete fissure fractures.

lines or zones represent distinct fissure fractures of the cortex due to local injury in the presence of a pathologic osseous system, and should not be confused with similar zones noted roentgenologically in cases of osteomalacia, osteitis fibrosa cystica, osteogenesis imperfecta and late rickets. Schmorl further advances the theory that the occurrence of these fissure fractures is responsible for the elongation of the long bones seen in Paget's disease, owing to the fact that these fairly wide fissures afford space for the formation of new bone along the convex side of the affected bone.

It is our belief that roentgenologists and surgeons in general are quite unfamiliar with the entity of these fissure fractures in Paget's disease and also with their clinical significance. This unfamiliarity is probably due to the fact that the literature is comparatively barren of actual case reports of this condition and also to a lack of observations made on such cases over a prolonged period of time. The following 4 cases of Paget's disease exhibiting fissure fractures are presented after having been carefully studied at intervals over a period of as long as three years. Two of these cases have been under the authors' personal observation, while the other two cases have been kindly loaned to us by Dr. E. P. Corson White, and Dr. Ralph S. Bromer.

REPORT OF CASES

CASE 1. J. D., a white male, aged sixty-one, was seen by one of the authors (R.L.J.) on April 11, 1934. His chief complaint at that time was pain in the left thigh. His history stated that on February 28, 1934, while running from a trolley car in order to get to work on time, he heard a distinct snap in his left leg. That night he noticed a peculiar twitching sensation in the left thigh and leg and found that on attempting to stand the leg felt weak and gave away under him, while at the same time a localized area of pain developed in the thigh. This pain persisted despite the use of liniment and baking and massage. On March 11, 1934, the patient was

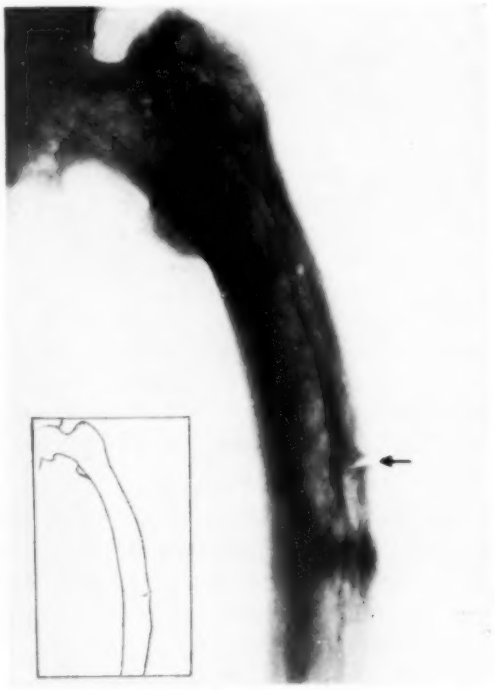

FIG. 2. Case 1. Two of the original incomplete fissure fractures have completely healed, while one is still present.

referred for a roentgen examination, which revealed a marked bowing of the left femur, together with the other characteristic features of an advanced Paget's disease. Along the convex surface of the bone at the junction of its middle and upper thirds there were noted three transverse lines of rarefaction which represent three incomplete fissure fractures (Fig. 1). The patient was admitted to the hospital and a brace applied to the left leg. Additional roentgen studies revealed marked evidence of Paget's disease involving the bones of the skull and the left half of the bones of the pelvis. It was also found that the blood Wassermann was plus 4. With rest of the involved leg the pain in the thigh slowly disappeared. The patient was discharged from the hospital on May 1, 1934, with instructions to continue wearing his brace. A roentgen examination, made on December 5, 1935, revealed a persistence of one of the lines of fissure fracture, while the other two fissure fracture lines had almost completely disappeared (Fig. 2). The patient was not seen again until February 2, 1936, when, while wearing his brace, he slipped on an icy sidewalk and fell, sustaining a complete transverse fracture of the femur at the junction of the middle and upper thirds. A roentgen examination made on the day of his admission to the hospital (Fig. 3) shows the transverse line of fracture to be an extension of the persistent fissure fracture line which was previously noted in the roentgenograms made on September 7, 1935. The fracture was reduced, a cast applied, and the patient discharged on May 2, 1936, at which time he was allowed the use of crutches. The final roentgen examination, made on January 29, 1937, revealed that the fragments had firmly united in good position and with little resultant deformity, while all evidence of the persisting fissure fractures had largely disappeared (Fig. 4).

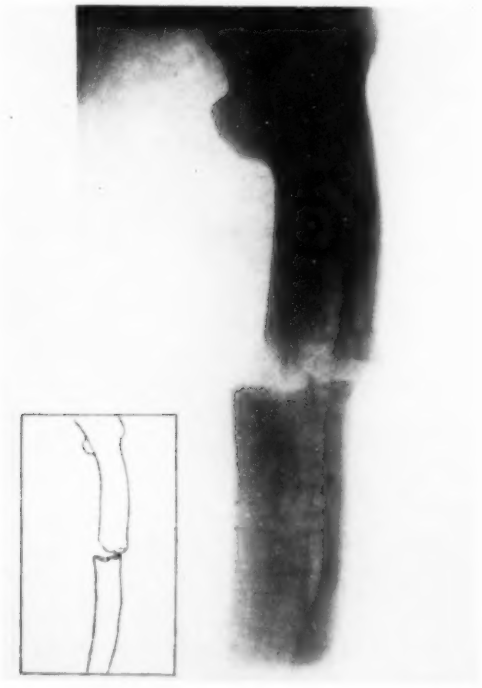

Fig. 3. Case 1. There is a complete transverse fracture of the femur following slight trauma. The line of fracture is an extension of the persistent incomplete fissure fracture seen in Figure 2.

Fig. 4. Case 1. The complete fracture has healed with little resultant deformity and all evidence of the preceding fissure fractures has disappeared. The callus has been transformed into bone characteristic of the dominant Paget's disease.

Case II. L. D., a white female, aged sixty-six, was first seen in the Orthopedic Dispensary of the Hospital of the Protestant Episcopal Church in May, 1933. Her chief complaint at that time was a dull aching pain in the right tibia which had been present for approximately one year. A roentgenogram made on May 23, 1933 (Fig. 5), revealed a marked bowing of the right tibia together with the other character-

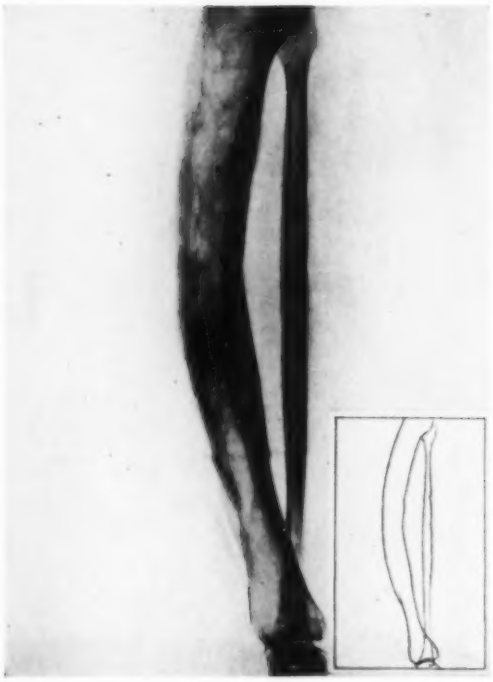

FIG. 5. Case II. Marked bowing and enlargement of right tibia with marked cortical thickening.

istic evidences of an advanced Paget's disease involving this bone. Additional films revealed the bones of the pelvis, lumbar spine and left femur to be involved by the bony dystrophy. A brace was applied to the right leg with relief of her symptoms. On April 2, 1935, while running to catch an elevated train, her right leg suddenly gave way under her despite the support of the brace, after which she found that she was unable to stand. She was admitted to the Hospital of the Protestant Episcopal Church on that date and a roentgen examination revealed two incomplete fissure fractures involving the convex surface of the right tibia (Fig. 6). The brace was reapplied to the affected leg and the patient was discharged from the hospital on April 5, 1935. She continued to wear the brace and was again examined roentgenologically on June 10, 1935. At that time it was noted that the lines of fissure fracture were still present and one of the lines had apparently become complete in nature, in that it extended transversely across the entire shaft of the bone (Fig. 7). There was a gradual subsidence of the pain in the affected leg and a final roentgen examination made on February 11, 1937, demonstrated that the lines of fissure fracture had almost entirely disappeared (Fig. 8).

CASE III. C. K. W., a white male, aged sixty-four, consulted a physician (Dr. E. P. C. W.) on October 26, 1934, because of lameness and pain in both legs. He stated that the lameness began five years before and had slowly but very definitely increased. A roentgen examination revealed an advanced Paget's disease of the skull, both femora, and both tibiae. The right femur, which was markedly bowed, showed four translucent lines on its convex surface (Fig. 9) which represented incomplete fissure fractures. There was no definite history as to when the patient sustained these incomplete fissure fractures. A brace was applied to the leg and to date the patient has not sustained a complete fracture of this femur.

CASE IV. J. M., a white male, aged seventy-six, and a store-keeper by occupation, had noticed that he was becoming lame when he was forty-eight years of age. This lameness, which was without pain, he attributed to his sedentary life. Five years later he began to have pain in his leg and lower back, because of which he

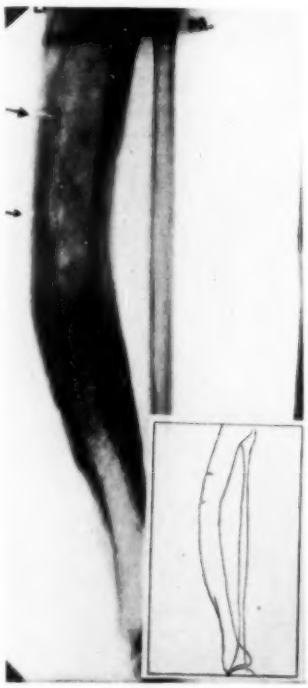

FIG. 6. Case II. There are two translucent lines involving the cortex on the convex surface of the tibia which represent two incomplete fissure fractures. These were caused by slight trauma.

consulted a physician. A diagnosis of Paget's disease was made at that time and a brace was applied to the involved leg. Since then the disease has steadily progressed and the patient has been compelled to do much of his work seated in a chair. An examination made on April 3, 1936, revealed a marked bowing of the right femur, together with the other typical appearances of an advanced Paget's disease involving this bone. Along the convex surface of the bone, in approximately its upper third, there are noted six translucent lines representing old, incomplete, fissure fractures, which are undergoing healing (Fig. 10). It has not been possible to determine when or how these incomplete fissure fractures were sustained.

From a study of the foregoing cases we are led to believe that fissure fractures occurring in Paget's disease are due to slight trauma and hence may be regarded as incomplete pathologic fractures. Such was the causative factor in Cases I and II and the fractures manifested themselves clinically by a sudden pain in the affected bone

Fig. 8. Case II. All evidence of the preceding incomplete fissure fractures has largely disappeared.

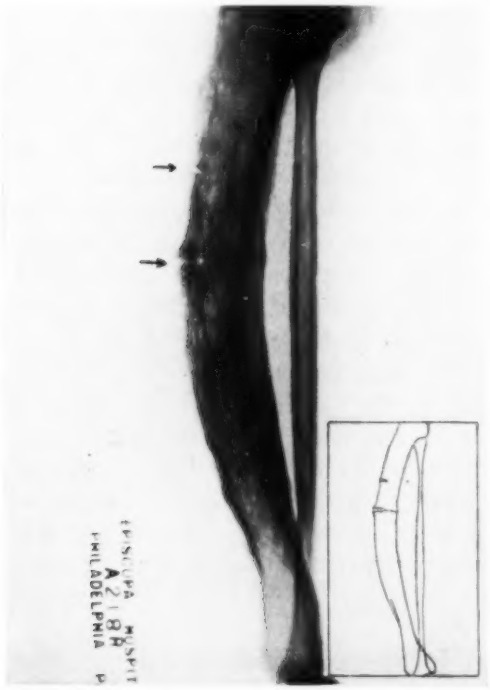

Fig. 7. Case II. The two incomplete fissure fractures are still present but are undergoing beginning healing. Note that the distal fissure fracture line has extended entirely across the shaft of the bone.

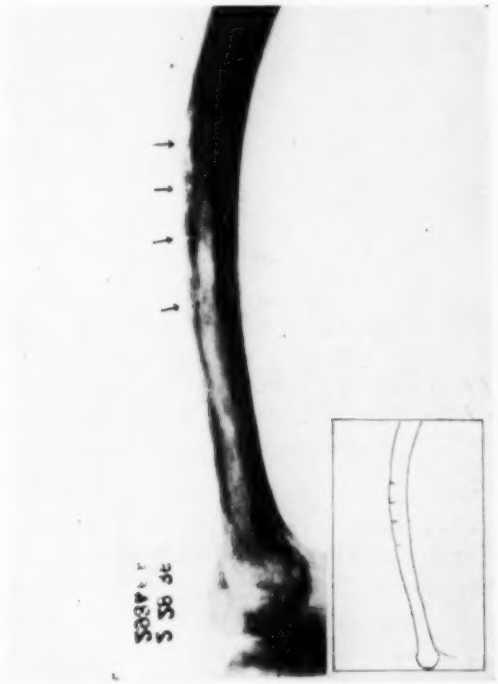

Fig. 9. Case III. There are four incomplete fissure fractures involving the cortex on the convex surface of the femur. The latter bone shows marked bowing and enlargement with thickening of the cortex.

and a distinct, persistent, localized tenderness. When one considers the brittle chalk-like consistency of the involved long bones in a case of marked Paget's disease, it is readily conceivable how such fissure fractures can occur, and how with additional slight trauma such fractures may go on to completely traverse the shaft of the bone and become complete in nature. The fact that they always occur on the convex surface of the markedly curved, weight-bearing bones is due to the fact that longitudinal forces transmitted through the shaft of the affected bone produce a maximum stress and strain on this surface, just as the point of maximum stress of a taut bow is always on its convex surface. The resultant cracking or fissure is very much like the similar phenomenon produced by the bending of an over-ripe banana, as the Germans have so aptly expressed it. Once produced, these fissure fractures do one of two things—they either result in a complete pathologic fracture, if there be additional trauma, or with the cessation of trauma they go on to complete healing, with a minimum amount of bone callus formation. As the callus goes through the various stages of calcification and ossification, according to Jaffe[3] it becomes involved in the pathologic process of the underlying bony dystrophy and the new bone shows roentgen evidence of Paget's disease. With the passage of time and a completion of healing, all evidence of the preceding fissure fractures becomes obliterated, although such fractures probably are responsible for a lengthening of the involved bone.

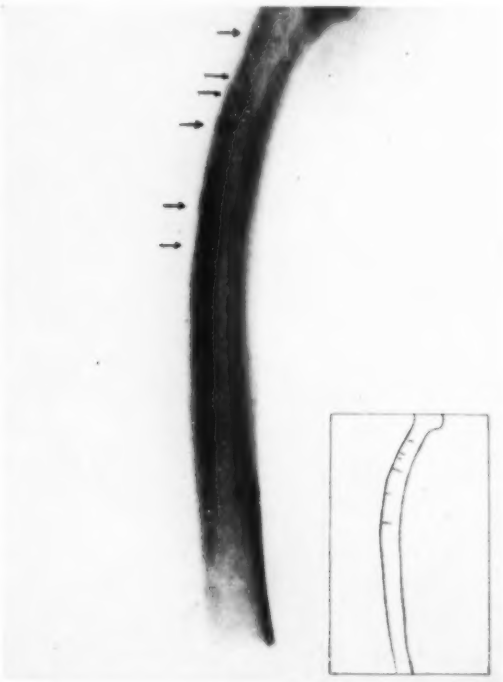

FIG. 10. Case IV. There are six indistinct, incomplete, fissure fracture lines involving the cortex on the convex surface of the proximal third of the femur. These are undergoing healing and are beginning to be obliterated by the dominant Paget's disease.

From a clinical standpoint it is important that roentgenologists and surgeons should be on the alert for the detection of fissure fractures in all patients with known Paget's disease, as such fractures are often the precursors of complete fractures. This is of particular importance when it is considered that Schmorl[8] found evidence of Paget's disease in 3 per cent of all autopsies in patients over forty. The proper treatment consists in the avoidance of active, vigorous exercise and the proper protective bracing of the affected limb, with frequent roentgenologic examinations to make sure that the fractures are properly healing. According to Maes,[5] patients with Paget's disease are prone to develop sarcoma at the site of old fractures, as he thinks that the regenerated bone has a special predisposition to sarcomatous changes. We have had no experience with this phase of the disease but merely point out the possibility of such a sequel to fractures in this bony dystrophy.

SUMMARY

1. Incomplete fissure fractures occur on the convex surface of the curved long bones in cases of marked Paget's disease, particularly the femur and tibia. They are manifested roentgenologically by one or more translucent, transverse lines through

the cortex of the involved bone. Pathologically these lines or fissures represent a dissimilar process than similar lines or fissures seen in cases of osteomalacia, late rickets, osteitis fibrosa cystica or osteogenesis imperfecta.

2. These fissure fractures occur following slight trauma and are due to the brittle, chalk-like consistency of the involved bone.

3. These fractures, which are incomplete in nature, generally heal with a minimum amount of bone callus formation, which assumes the characteristics of the dominant Paget's disease. However, with additional slight trauma, they may go on to complete fracture, which is always characteristically transverse in nature.

4. Patients with known Paget's disease should be watched for the occurrence of fissure fractures as they are often danger signals that a complete fracture may occur. When such fissure fractures do occur, they should be treated with appropriate rest and splinting or bracing.

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RADIATION TREATMENT OF EPITHELIOMA OF THE LIP*

By WENDELL C. HALL, M.D.
PHILADELPHIA, PENNSYLVANIA

ROENTGEN and radium therapy were in their infancy when the first epithelioma of the lip was treated in the radiological department of the Hospital of the University of Pennsylvania in 1908. The gradual increase in knowledge of radiation therapy is reflected in a slow but consistent improvement in technique in treating the 285 cases since that date. The first patient treated twenty-eight years ago had an advanced lesion of the lip with metastasis to the neck. It was obvious that he was sent to the radiological clinic only because his condition was considered hopeless and not amenable to other forms of treatment. Needless to say, radiation treatment did not give a brilliant result in this first case. Nor was this the only patient turned over to this department or to other radiological clinics during the early years because of lesions so far advanced that no one else wanted to treat them. Such cases, of course, helped to give the impression that results from irradiation were not very successful. As the radiologist has seen less advanced cases, however, his results have correspondingly improved, and now radiation treatment to the average local lesion on the lip is equally as good as surgery in preventing a recurrence and is decidedly better as far as the cosmetic result is concerned. Furthermore, both the inconvenience and the cost of hospitalization for a surgical procedure are unnecessary when roentgen rays or radium can be used so successfully.

Clinically, there is nothing particularly unusual about these 285 cases. With the exception of 3 Negroes, all the patients in the group were white. The majority of the lesions occurred in men, only 6.3 per cent being in women. The lower lip was involved in 82.5 per cent of the cases, the upper lip in 13 per cent, the corner of the mouth in 3 per cent, the upper and lower lips in 0.35 per cent; the position of the lesion was not stated in 1.5 per cent of the cases. Although the lower lip was involved in 88 per cent of the men, the upper lip was involved in 77.7 per cent of the women—almost the reverse incidence in the two sexes. No conclusive arguments have ever been advanced as to why one lip should be involved more frequently than the other, nor does a study of these cases offer any satisfactory explanation. It remains an unexplained fact that the lower lip is much more frequently involved than the upper lip, and it seems inconsistent that the opposite should be true in about three-fourths of the women in this series.

Biopsies were done on approximately one-half of these cases. They were frequently omitted in the beginning of the series but within the past several years they have been essentially a routine. Almost all the lesions were squamous cell in type. Basal cell lesions occurred as frequently on the lower as on the upper lip.

Irritation and exposure to weather appeared to be predisposing factors in causing these epitheliomas of the lip. Farmers, laborers, carpenters, incessant pipe smokers, persons with leukoplakia, and those with jagged teeth sought treatment most often. The onset of the lesion could be traced to trauma in a few instances. A family history of malignancy appeared to be of no significance. The age of the patient, however, seemed important. Most of the patients in the group were over fifty years old when they first came to the clinic, and the highest number of lesions occurred in the fifth, sixth, and seventh decades. Although the youngest patient was nineteen years old, only 2 per cent of

* From the Department of Radiology, Hospital of the University of Pennsylvania, Philadelphia.

the group was under thirty years of age.

The large majority of these patients reported for medical assistance within the first year after the appearance of the lesion. Unquestionably, however, the prognosis in an individual case depended solely upon the particular lesion itself rather than on the length of time the lesion had been present. A singularly bad prognosis attended those cases which had metastasis when they first came to the clinic.

It is more difficult to follow up patients having cancer of the lip than it is to follow up those having malignancy of other types. There are several apparent reasons for this. Some of these patients lived two or three hundred miles away, and the expense of returning, in addition to the time required, made it impractical for many of them to keep subsequent appointments. Furthermore, once the local lesion is cured, it is difficult to convince a patient that he has any other cause for concern, and he may therefore fail to see the necessity of returning for periodic observations. Usually a patient continued to keep his appointments at least as long as he was having any trouble; and even after disappearing from observation for a year or two, many of them returned very promptly if they suspected a recurrence of the old lesion. This would seem to indicate that in many instances a failure to keep an appointment probably meant that the patient was free of the disease. In spite of the difficulty in getting patients to keep their appointments, many of them continued to return for more than five years and some of them for as much as fifteen years or longer.

Methods of treating epitheliomas on the lip have slowly but steadily improved in this clinic since 1908. Prior to 1927, only a few local lesions were treated with roentgen rays; the remainder were treated with radium. The average local lesion received one or two applications of radium, some of the doses being as low as 25 mg-hr., and only a few of them exceeding 200 mg-hr. Immediately following this radiation treatment approximately one-half the local lesions were electrodesiccated. The latter was a wise procedure in view of the small doses of radium, and the results would undoubtedly have been less successful without it. Since the radium was only filtered through 0.3 mm. alloy, or 0.5 mm. aluminum or silver, even the small doses must have given marked reactions because of the excessive percentage of beta radiation on the skin surface.

The radium filtration was increased to 1.5–2 mm. brass in 1928, and this change in technique made it possible to give considerably larger amounts of radiation to the local lesion. Doses of 400–2,000 mg-hr. now became the rule. Electrodesiccation was no longer necessary as a supportive measure, and for the first time the radium treatment gave uniform assurance that it was sufficient in itself to cure the average epithelioma on the lip.

During the latter part of 1932, a few of the lesions were treated with superficial roentgen therapy, and in 1933 radium was discarded entirely since results with roentgen therapy were so successful. The choice of roentgen rays in preference to radium in recent years is not due to any better curative value of one form of irradiation over the other, but to the fact that the roentgen dosage can be given in a shorter time, and can be applied more evenly and measured more accurately. Treatment factors from 1933 to 1936 were as follows: 135 kv., 5 ma., 30 cm., 7,000–10,000 r, approximately two-thirds unfiltered and the other third filtered through 1 mm. aluminum. Occasionally two or three portals were used, giving 3,600–7,200 r to each portal. In 1936, a Siemen's contact therapy machine was installed and this has been used on the few patients who have appeared for treatment since then. The factors for this machine are as follows: 50 kv., 4 ma., 0.2 mm. copper filter, 3 cm. distance, 5,000–10,000 r in two to four sittings.

During the entire period from 1908 until the present, prophylactic irradiation has

been administered to the neck. Radium, first filtered through as little as 2 mm. aluminum and later through as much as 2 mm. brass, was used as a supplementary measure in treating the lymphatic drainage areas until 1931. However, chief reliance was placed on roentgen irradiation to the neck during this entire period, the doses ranging from 500–1,500 r to one or both sides of the neck immediately after treatment of the local lesion. Superficial therapy was used most of the time although an occasional case was treated with deep therapy. Every radiologist is familiar with the fact that even large blistering doses of roentgen rays to metastatic nodes in the neck are seldom of any value when used alone, and at best these small doses as a prophylactic measure are of questionable value. Still, it is conceivable that occasionally an embolic cancer cell may be killed in this manner, and, if so, it is worth the small effort to give this amount of radiation to the neck, especially since the patient experiences no discomfort as a result. However, one slight disadvantage arises if the patient later develops metastasis to the neck, since less external irradiation can subsequently be given to supplement any surgical or implantation procedure.

A cure of the local lesion on the lip is usually a relatively simple matter. There were only 10 local recurrences in this group of 285 cases; of these only 2 occurred during the past ten years, the last one in 1932. Even the recurrences were usually easy to cure. There is, however, the ever present danger that metastasis will develop, thereby making the prognosis much more grave. The seriousness of the prognosis in the metastatic cases is borne out by an analysis of the deaths among our patients. Thirty-seven patients died directly as a result of the malignancy, and 95 per cent of these died after metastasis had developed, only 2 in the group dying from the local lesion alone. Less than 5 per cent of the patients who developed metastasis were successfully cured, and it may safely be said that if a patient has moderately advanced metastasis to the nodes in the neck when he first seeks treatment, the chance of a cure is slight.

There is great confusion and diversity of opinion in the literature as to how the lymphatic drainage areas in the neck should be treated in the absence of metastasis. Even though no palpable nodes can be found, some writers advocate external irradiation with deep therapy in large blistering doses, and still others steadfastly advocate a routine block dissection of the lymphatics on the side of the lesion. A small but increasing number of radiologists and surgeons is beginning to realize that neither of these procedures is advisable when evidence of metastasis is lacking. All of our patients without metastasis received very conservative treatment, and the wisdom of this course can be supported substantially by an analysis of the cases. Two hundred and fifty-eight patients were free of metastasis at their first visit, and as yet only 8 of these (3 per cent) have developed metastasis in the neck after cure of the local lesion. It is granted that a few others may develop metastases later, but if a patient is going to get metastasis after cure of the local lesion, he will develop it in less than one year, in most instances. Nine months or less elapsed between cure of the local lesion and the appearance of metastasis in our 8 patients, and the majority of these 258 cases have been under observation over one year; hence few if any more of them are likely to develop metastasis. It seems apparent therefore that *if the local lesion is cured before metastasis develops, the likelihood of metastasis appearing later is somewhat remote.* What more convincing evidence does one need to show the folly of giving blistering doses of radiation, or of doing a routine block dissection of the neck in the absence of demonstrable metastasis? It must be remembered, too, that in spite of block dissection it is still not uncommon for metastasis to appear in the dissected area, and this might have occurred in any of the 8 patients who developed metastasis,

even if they had had dissections. Furthermore, an operative mortality which is anything but negligible must be taken into consideration, especially since many of these patients were more than sixty years old. Many attempts have been made to show the value of routine block dissection of the neck as a prophylactic measure. The excellent results reported in some instances may be attributed to the fact that most of the patients did not have and would not have developed metastasis, regardless of the dissection.

There is still other evidence to show that conservative measures in the absence of definite metastasis are more than justified. One hundred and fourteen patients had palpable nodes in the neck at their first visit, yet less than one-fourth of these proved to be metastatic. After starting treatment 43 more cases developed palpable nodes, only 8 of which later proved to be metastatic. Thus, there were 157 patients with palpable nodes in the neck at some time during the course of observation, yet in 77.7 per cent of them the nodes were benign. Many nodes which were palpable when the patient was first seen, or which became palpable just after the local lesion was treated, disappeared as soon as the local lesion was cured. Nodes of this type were enlarged by an inflammatory reaction and not by cancer cells. If radical measures had been used in their treatment slightly over three-fourths of these patients would have been unnecessarily subjected to such a procedure. At times, it is of course difficult to determine by physical examination whether a nodular enlargement is due to inflammation or to metastasis, but careful observation of the nodule for several weeks will do no great harm and will usually eliminate the doubt.

While the question of prophylactic treatment to areas in which metastasis may occur has caused much argument and diversity of opinion, this question is not nearly as important as that pertaining to the treatment of metastasis when it is actually present. Here, too, we feel that the methods used should be conservative. Only 2 of our cases had block dissection and these dissections were for advanced metastases which were present when the patient was sent to the clinic. Both patients were treated about fifteen years ago, and both of them died. According to present day methods they would have been considered inoperable, and would have received nothing more than large doses of roentgen rays to the neck, purely as a palliative measure. Although block dissection is usually of no value in cases of advanced metastasis, discrete metastatic nodes can be treated most successfully by surgery. This has been proved to our satisfaction in the treatment of several of our patients. External irradiation is a valuable aid to surgery in these cases, but it should not be used alone in view of the well-known high radioresistance of most of these metastatic nodes. Seldom is one of them seen to disappear under external irradiation alone. When the metastatic nodule is fixed to surrounding tissues, i.e. when the metastasis has penetrated the capsule of the lymph node, it is probably not advisable to attempt surgical removal for fear of leaving some of the malignant cells in the tissues. In these cases the metastatic area should receive about 5,000 r external irradiation and this should be followed by surgical exposure and visual implantation with radon or with radium needles containing 0.6 mg. of radium element to the running centimeter of needle filtered through 0.5 mm. platinum. Most attempts to implant radon or radium needles blindly through the skin without surgical exposure will be unsatisfactory. It is inadvisable to attempt either surgical removal or exposure and implantation of a metastatic mass which is very large. Such conditions are best treated by external irradiation, for it is better to use palliative measures here than to increase the discomfort or to hasten the death of the patient by doing anything which is in the least radical.

The above discussion may be summarized for the sake of emphasis and

clarity in a few concise rules which will be applicable in nearly all instances:

1. A routine block dissection of the lymphatics of the neck for epithelioma of the lip is impractical in the absence of metastasis because:
   a. A large number of patients with epithelioma of the lip never develop palpable nodes in the neck at any time.
   b. Most palpable nodes in these cases are benign.
   c. Very few patients develop metastasis after the local lesion on the lip is cured.
   d. An appreciable morbidity and mortality follows block dissection.
2. Routine prophylactic irradiation to the neck is probably impractical in the absence of metastasis because:
   a. A large number of patients with epithelioma of the lip never develop palpable nodes in the neck at any time.
   b. Most palpable nodes in these cases are benign.
   c. Very few patients develop metastasis after the local lesion on the lip is cured.
   d. Prophylactic irradiation, in amounts small enough to be practical, is probably not sufficient to cause the death of any cancer cells which may be present in the lymphatics. Such irradiation, however, may render the tissues of the neck less fertile for the growth of cancer metastases.
3. Local discrete metastases which have not perforated the node capsule should receive 3,000–5,000 r external irradiation, preferably by highly filtered deep therapy. At the appropriate time they should then be removed surgically. Such discrete metastatic nodes should not be treated by external irradiation alone because they are radioresistant in most instances. An alternative here is to give external irradiation and then follow this by surgical exposure and implantation with radon or radium needles. The former plan, however, is the better of the two.
4. Small fixed metastases should be exposed surgically and implanted with radon or radium needles after receiving 3,000–5,000 r external irradiation. No attempt should be made to remove them because of the difficulty in effecting a complete extirpation.
5. Extensive mass metastases should be given only palliative large doses of external irradiation, since there is no known method of cure, and any drastic measures will probably kill the patient or at least make his condition worse. Such radiation should be applied in daily small doses. Large doses tend to cause the center to break down and become necrotic, especially if there is a superimposed infection in the mass.

Except in advanced cases, the local lesion on the lip no longer offers any problem to the radiologist. The treatment of metastasis in the neck, however, varies widely, and it is here that the real problem lies. From a study of the cases in this group a few suggestions in treatment have been given, but it is to be hoped that before long there will be increased knowledge of the subject. More uniform and more successful results will not be observed until this knowledge is obtained.

SUMMARY

Two hundred and eighty-five cases of epithelioma of the lip have been treated in the radiological clinic of the Hospital of the University of Pennsylvania since 1908. A brief clinical survey of these cases is given, and the various methods of treating them are summarized. A plan for treating the lymphatics in the neck, before and after metastasis, is presented and substantiated by an analysis of the statistics obtained from a study of these cases.

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DUST HAZARD AMONG FOUNDRYMEN

By LESLIE H. OSMOND, M.D.
PITTSBURGH, PENNSYLVANIA

A CLINICAL and roentgenological survey of men working in a foundry was instituted by the far-seeing, socially minded executives of a heavy industry located in Pittsburgh to determine the status of lung pathology among their workmen. This was deemed advisable after a petrographic and dust count analysis showed that a definite silicosis hazard existed.

It was decided that the chests of applicants should be examined roentgenologically in order that those having latent or active cases of tuberculosis would not be allowed to work in a harmful silica dust atmosphere, a procedure which is now recognized as a distinct hazard to such individuals. Pre-employment roentgenological examination of the chest is also of value in detecting individuals who have developed silicosis with or without infection.

A roentgen-ray department has been installed in the company's hospital and the roentgen examination of the chest has been done at the same time as the annual medical examination. The roentgen examination of the chest has been presented to the workmen as just something additional to their regular examination.

PROCEDURE

A routine annual physical examination has been carried out by Dr. R. A. Campbell at the time of making the roentgen examination of the chest. Rather complete histories have been taken, especially in regard to the cardiorespiratory system. A complete occupational record of each man was available. The exact location of work of each individual in the plant since the time of employment by this company was known. Likewise, the dust counts of the atmosphere in the different locations were available. A standard exercise test has been done on all cases showing any lung pathology. This has consisted in having the individual step up and down from a chair twenty-five times. If the heart rate returned to normal in two minutes, the subject's cardiac compensation was considered adequate.

Some laboratory procedures have been carried out on these men. The vital capacity of all men, including applicants, has been taken. All individuals, showing roentgenological evidence of possible open tuberculosis, have had at least two sputum examinations. Most cases, showing evidence of superimposed infection, have had blood sedimentation tests.

A roentgenoscopic examination has been made on all cases. The range of each dome of the diaphragm has been measured. An estimation of the retrocardiac and preaortic spaces has been attempted. The contour of the spine has been inspected. The impression from the roentgenoscopic observation has been used as a guide in making exposures. Stereoscopic films have been routine. Films of increased density have been made in the cases of massive lesions and films of less exposure were employed to help in detecting evidence of silicotic fibrosis in the emphysematous lower lung fields.

TECHNIQUE

All films have been made at a target-film distance of 4 feet, with a 2 mm. focal spot on a rotating anode using 400 ma. for 1/30 sec. exposure. The kilovolt (peak) has ranged from 54 for an 8 inch chest to 76 for a 12 inch chest. The energizing unit was a three-phase type of generator. Films made in this manner have been uniformly of excellent detail.

METHODS OF SAMPLING AND ANALYSIS

The Industrial Health Section of the Metropolitan Life Insurance Company

made a chemical and dust count analysis, which was supervised by J. Wm. Fehnel, on February 2 to 5, 1934. Chemical analysis of a representative sample of the air-borne dust in the foundry showed approximately 52 per cent free silica and 10.3 per cent calcium and magnesium silicates, making 62.3 per cent total silica content.

The dust samples were taken by the methods and technique developed and used by the United States Public Health Service.[10] The counts of particles less than 10 microns in size were made by the light field method.

Particle size measurements were found by making a photomicrograph under a high dry magnification and further enlarging the negative by projection.[4] It was determined that 95 to 99.3 per cent of the particles of dust were less than 10 microns in their greatest diameter.

CLASSIFICATION OF CASES

An attempt has been made to separate the cases according to the classification prepared by a committee composed of Sayers, Pancoast, Pendergrass, Lanza, McConnell, Riddell, Sampson and Gardner.[8]

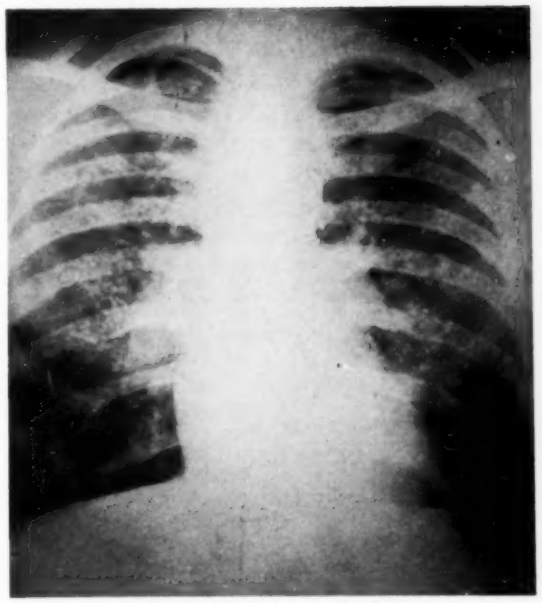

Fig. 1. More or less regular nodulation of infection throughout all lobes with sharply defined nodules 1 to 2 mm. in size diffusely interspersed.

Many cases showing irregular exaggeration of the linear markings, with and without beading confined to the trunk, and cases with increased root shadows have been classified as having healthy lungs and adnexa.

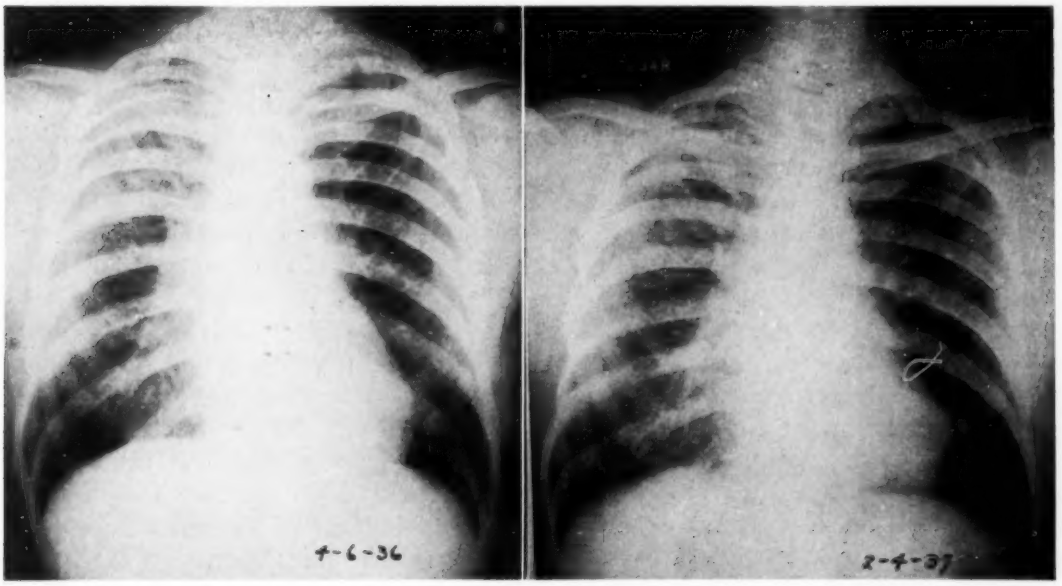

Fig. 2. Progression of tuberculosis superimposed on silicotic fibrosis.

The great majority of the cases of simple silicosis showed definite linear exaggeration with scattered discrete fine nodules 1 to 2 mm. in diameter. There were 4 cases showing discrete nodules 3 to 6 mm. in diameter. Serial examinations may necessitate placing these with silicosis plus infection. There were no cases that I was willing to classify as a conglomerate type of reaction. All such reactions in this group were placed, without much hesitation, in the group of localized shadows of increased density in the upper lobes. Progression has been noted in practically all nodules in 2 cases, as shown in Figure 2.

These cases are to be contrasted with a miliary nodulation of tuberculosis without exposure to silica dust. Such cases are usually prostrated or nearly so and run a rapid downhill course. One man (Fig. 2) has worked ten months since the first examination. Recently he was placed on

TABLE I

DISTRIBUTION OF CASES AND DUST COUNTS

Years of service	Coremakers				General Iron Foundry				General Steel Foundry				Steel Foundry Chippers				Iron Foundry Chippers				Molders				Cranemen				Open Hearth			
	1 to 15	16 to 20	21 to 25	26	1 to 15	16 to 20	21 to 25	26	1 to 15	16 to 20	21 to 25	26	1 to 15	16 to 20	21 to 25	26	1 to 15	16 to 20	21 to 25	26	1 to 15	16 to 20	21 to 25	26	1 to 15	16 to 20	21 to 25	26	1 to 15	16 to 20	21 to 25	26
Healthy lungs and adnexa	35	7	5		48	4	2		132	12	6	1	56	9	6	1	9	2	2		52	17	12	5	79	11	3	2	40	13	1	2
Simple silicosis		1	2	2			1			1	3	1		2	3	2					1	1	6	7				1				1
Silicosis with infection										2	2			10	4			1	1			1	3					1				
Probably active tuberculosis		1			1				3	3	1		8	1			1				1	1	1		3				1			
Probably arrested tuberculosis	5				1				1			1	4	1			1	1	1		1				11	2			1	2		1
Dust count* per cubic foot	44.9 million				35. million				16.4 million				19.6 million				35. million				13.1 million				42.6 million				Less than 16.4			
									240 million during night shakeout																165 million during night shakeout							

* The counts were made on February 2, 1934. The activity in this foundry was greater in 1934 than at any previous year.

silicotics with infection. This left no case of massive fibrosis due to the inhalation of silica dust per se.

In 5 of the silicotics with infection, there was a more or less regular nodulation throughout all lobes with the peripheral portions relatively free of nodules. The nodules varied from 3 to 8 mm. in diameter. The central portions of the smaller nodules were dense and sharply outlined simulating the silicotic nodules, which were diffusely interspersed throughout the lower three-fourths of each lung field. These central portions were surrounded by an ill-defined halo of lessened density. Some were definitely soft in character. Such cases are represented in Figures 1 and 2. Two of these cases were associated with larger permanent disability, and he resented being considered unable to work.

The remaining 20 cases of silicosis with infection showed processes which are usually regarded as typical of the usual forms of tuberculosis. There was one cavity.

In 19 of all cases of silicosis with infection, the presence of active infection has been fairly well established by increased sedimentation rates, persistently elevated afternoon temperatures and by demonstration of definite progression of lesions within the last six to twelve months. By the same evidence, activity has been fairly well established in 7 of the 26 cases listed in Table 1 as suspicious of having probably active lesions. Sputum examinations have been done twice on nearly all of the cases.

These were all negative so this procedure will be omitted in all future work on these men. It is probable that many of these men purposely did not get true sputum specimens, although they were well instructed.

ANALYSIS OF RESULTS

There was a total of 990 men examined in this survey. Some of these men have not been exposed to dust containing silica at all and there were not sufficient data on some of the foundry men to include them in a detailed study. As there were some silicotics with and without infection, the results should not be altered appreciably by leaving this group out.

An analysis has been made of 686 men* who have been exposed to a supposedly harmful concentration of dust containing silica. There were 38 cases, or 5.5 per cent, with simple silicosis; 25 cases, or 3.6 per cent, with silicosis and infection; 26 cases, or 3.8 per cent, with probably incompletely arrested or active tuberculosis; 34 cases, or 4.9 per cent, with apparently arrested adult type of parenchymal tuberculous lesions; and 104 cases, or 15.1 per cent, showed irregular exaggeration of the linear markings of which 17 cases, or 2.4 per cent, of the total showed a minimal but definite beading confined to the trunks.

The percentage of cases in the whole group really means very little as a large proportion of the men have worked less than five years in the foundry. The incidence of simple silicosis increased from 5.5 per cent for the whole group to 19 per cent for all men working in the foundry sixteen years or over and to 32.2 per cent for all men working twenty-one years or over. Silicosis with infection increased from 3.6 per cent to 13 per cent and 12.2 per cent respectively, making a total of 44.4 per cent showing definite evidence of silicotic fibrosis in the lungs after twenty years of exposure. An additional 30 per cent of the total group exposed more than twenty years showed an irregular exaggeration of the linear markings, with and with out beading confined to the trunks.

Table I shows that there was considerable variation in the concentration of dust to which the various groups of workmen were exposed, and Table II shows that there is considerable variation in the number of silicotics as compared to the concentration of dust. The highest incidence of simple silicosis is among the coremakers who have worked in the highest concentration of dust, but the molders show an incidence closely approximating that of the coremakers, and they have been working in a comparatively low concentration. The cranemen and iron foundry chippers show a very low incidence of simple silicosis, but they have been working in a comparatively high concentration of dust. The

TABLE II

INCIDENCE OF SILICOSIS WITH AND WITHOUT INFECTION IN ALL MEN WHO HAVE HAD 16 YEARS, OR MORE EXPOSURE

	Million Particles of Dust per cu. ft.	Simple Silicosis	Silicosis with Infection
Craneman	42.6	5.5%	5.5%
Molders	13.1	25.4%	7.4%
Steel foundry chippers	19.6	18.4%	36.8%
Iron foundry chippers	35.		33.3%
General steel foundry	16.4	15.6%	12.5%
General iron foundry	35.	14.2%	
Coremakers	44.9	27.7%	
Open hearth	less than 16.	5.5%	

* All white males.

incidence of silicosis with infection is just as erratic in its distribution. There is a high incidence among the steel foundry chippers. There is also a high incidence among the iron foundry chippers, but this is a very small group of men and is not of much comparative value. In the general iron foundry and the coremaking departments, there are no silicotics with infection although the dust concentration was relatively high. This distribution of cases suggests that one cannot determine the dust count and predict the relative incidence of silicosis with or without infection.

The above findings agree with past experience, which was emphasized by Cummings at the Second Symposium on Silicosis held in connection with the Trudeau School of Tuberculosis. He stated that the determination of dust concentrations in any given industry did not afford an accurate method of evaluating a dust hazard, but rather that the routine medical examinations and satisfactory roentgenograms of the chest of employees furnish the only accurate means of determining the presence and severity of an actual hazard.

After due consideration of many factors, Cummings[1] has described a "primary threshold." This consists of many years' exposure of a normal man to 5,000,000 pure crystalline silica dust particles per cubic foot, as determined by the light field counting method, without impairing his health. On the basis of 52 per cent free silica, approximately 9,600,000 particles would be the "primary threshold." The departments included in this survey had dust counts ranging from 13.1 to 44.9 million particles,* which are greater than the "primary threshold," and there is a definite incidence of silicosis after sixteen years' exposure.

In an investigation of granite cutting plants,[9] most of the workers were found to be exposed to an average of 60 million particles of dust less than 10 microns in size. The dust contained about 70 per cent total silica, of which about 35 per cent was in the form of free silica. A probable safe limit of between 9 and 20 million particles could be established. On the basis of 52 per cent free silica, the probable safe limits would be in the range of 6 to 13.2 million particles. As pointed out above, the molders in this survey have been exposed to 13.1 million particles and there is an incidence of simple silicosis of 25.4 per cent among those with sixteen years' or more exposure and it rises to 58.3 per cent among those with twenty-one years' or more exposure. Of course, comparison of dust counts in the granite cutting industry may not be justifiably compared to those in the foundry.

Practically all of the men are now wearing respirators and their efficiency is demonstrated by the following counts. While the dust at the level of the crane runners was 42.6 million particles, it was 39.3 million particles beneath the respirator with an old cartridge and 12.2 million particles with a new one. If the men would wear these respirators continuously, and keep a reasonable maintenance, the greater portion would be working in dust concentrations well below the "threshold limit" of Cummings and the Wisconsin Code, which provides that the maximum concentration of dust containing 35 per cent silica shall be 15 million particles. The smaller remaining group of men would be slightly over this basal limit.

SILICOSIS AND RESPIRATORY INFECTION

In the past eight years, there have been 86 deaths in workers from the foundry. The death certificates listed 16 as due to tuberculosis, 19 as due to lobar pneumonia and 8 as due to bronchopneumonia. The yearly average of men working in the foundry for the same period was 387. Using these figures to compute a comparable rate, there have been 517 deaths per 100,000 as compared to 89 per 100,000 for all males in Allegheny County over thirty years of age. With 27 deaths due to pneu-

* The steel foundry has a high dust concentration during the night shakeout. There are few men working at this time (see Table 1).

monia in eight years, the yearly rate was 872 per 100,000 as compared to 186 per 100,000 in Allegheny County. The death rate from tuberculosis and pneumonia in this foundry appears to be definitely greater than that of the general male population over thirty years of age in the surrounding community.

Twelve of the 16 deaths from the foundry in the last eight years have been from the steel chipping department. Tables I and II show that there is now a high incidence of probably active tuberculosis and silicotuberculosis in this group and a large percentage of these cases are well advanced. These facts suggest that there was one or more definitely open cases of tuberculosis in this department years ago and that there is a certain amount of exogenous character to the infection among the present group.*

There are a few cases which show excessive apical pleural thickening with fuzzy irregular margins. There are ill-defined nodules in the adjacent lung parenchyma. These are less numerous in each upper lobe, the greater the distance from the apical caps. These cases suggest possible reactivation of apical caps.

Figure 3 shows the best example of the above group. This man, aged forty-eight, does not admit any symptoms. He has been working in the steel chipping department for eighteen and a half years. The excursion of each dome of the diaphragm was within normal limits (7 cm.), but the vital capacity as measured by the McKesson respirometer was 80 per cent as figured from the height and 82 per cent as figured by weight. Two sputum examinations were negative for tubercle bacilli. One morning temperature was 98° F. Two afternoon temperatures one week apart were 100.3° and 99.6° F. The sedimentation rate was 18 mm. in forty minutes. The urine examination was negative. This case has been classed as active tuberculosis. If this case and the others similar to it represent reactivation of the apical caps, they agree with Gardner's[3] work showing that apical lesions break down and give rise to a very chronic silicotuberculosis.

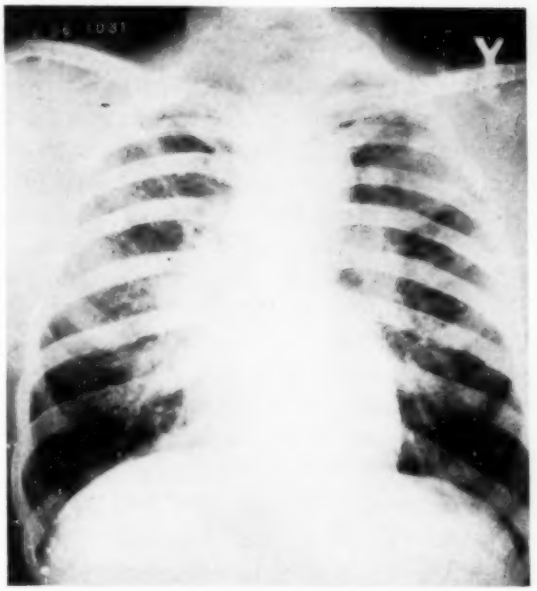

Fig. 3. Possible activiation of apical pleurae. Excessive apical pleural thickening with fuzzy irregular borders and numerous ill-defined nodules adjacent in both upper lobes.

PHYSIOLOGICAL CONSIDERATIONS

The vital capacities, exercise tests and ranges of diaphragmatic motion in the group with simple silicosis do not differ appreciably from those with healthy lungs in the same age group, but this group shows an early to moderate silicotic fibrosis. These tests in more advanced cases would probably show definite evidence of pulmonary pathology. In the few cases that had marked emphysema there was a definite reduction in the vital capacity. There was a corresponding deficiency in cardiac response to work and a decrease in range of the diaphragm to 2 or 4 cm.

There was a high percentage of those with silicotuberculosis and apparently active tuberculosis which showed a definite decrease in vital capacity, range of motion of the diaphragm and cardiac response to

* It has recently been learned that most of the men, who have probably active tuberculosis with and without silicosis associated, worked in intimate relationship with nine of the 12 men who have died in the last eight years from tuberculosis. The original group of nine men were all bachelors and lived under the same roof for years.

work. This was no more than one would expect.

The only value of these tests has been in helping to show that with few exceptions the individuals with early to moderate silicotic fibrosis do not have any decreased capacity for work, which cannot be ascribed to age and cardiovascular degeneration.

If one could know the normal range of the diaphragm and the normal vital capacity for each individual, these tests would be of much more value in this work. An intensive study of individuals along the lines which have been outlined by Hurtado, Kaltreider, Fray, Brooks and McCann[5,6,7] should give valuable information concerning functional disability among pulmonary fibroses.

SUMMARY

Regardless of the history of exposure to dust, a diagnosis of silicosis has not been made unless generalized discrete nodular shadows were visible in the lung fields. The nodules were small, suggesting that silicosis among foundrymen is different from that in granite cutters, sandblasters and iron miners. The difference is probably due to the relatively low dust concentration to which they are exposed. All of the large localized shadows of increased density have had certain factors which placed them in the group of silicosis with complicating infection. The generalized nodules of infection in all lobes or in both upper lobes were quite prominent.

Few cases of pulmonary infection have been detected by the necessarily cursory physical examination. The sputum examination has been of no value in this survey. Sedimentation rates have been of value in ascertaining the presence of active infection. Detection of progression of the lesions by roentgenograms has been of distinct value and will eventually give the most reliable information.

With few exceptions, the men with simple silicosis have no apparent limitation of their working capacity, but these men show only an early to moderately advanced fibrotic process. With the introduction of efficient respirators, provided the men wear them and keep a fair maintenance filtration efficiency, the hazard of simple silicosis per se should be nil. All cases of active infection are being removed from duty. In time, these procedures, together with elimination of poor risks among applicants, promise to reduce the dust hazard in this foundry from its present prominent place as regards superimposed tuberculosis to a minimum.

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THE RADIATION TREATMENT OF HYPERTHYROIDISM*†

A REPORT OF THE RESULTS AT THE HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA DURING THE SEVEN AND ONE-HALF YEARS ENDING JULY 1, 1934.

By JOHN H. HARRIS, M.D.
HARRISBURG, PENNSYLVANIA

I. INTRODUCTION

THE purpose of this paper is to evaluate the results of radiation therapy in hyperthyroidism. During the past eight years, 350 patients have been treated by the Department of Radiology of the Hospital of the University of Pennsylvania. These patients have been carefully studied before and after treatment by Dr. Edward Rose and his associates in the Thyroid Section of the Medical Service of the hospital. The supervision of the patients by the medical service leads to a more nearly unbiased judgment of the results than could be expected otherwise.

II. PHYSIOLOGY, PATHOLOGY, CLASSIFICATION

Although the thyroid gland has been extensively studied in regard to its normal and abnormal structure and physiology, much remains to be learned concerning it. Marine[20] states that the function of this gland is to provide the means through its iodine-containing hormone, thyrotoxin, for maintaining the higher rate of metabolism or oxidation process than would otherwise exist and that through fluctuation in activity it provides a means of varying the rate of metabolism to meet changing physiological needs. Boyd[5] says it is easy to say that the gland exerts a potent and far-reaching influence over the various processes of body metabolism, of oxygenation in particular, but how this is actually done cannot be answered.

As it became evident that thyroid disease could not be classified upon the basis of the microscopic finding, a classification[38] has been generally adopted which is based upon the aspect of the patient. Such a classification divides the abnormal gland into (1) diffuse non-toxic, (2) diffuse toxic, (3) nodular non-toxic and (4) nodular toxic. Boyd, Reinhoff and Dunhill (quoted by Martin and Elkin)[21] divide goiters into (1) diffuse goiter with involution (adolescent and colloid), (2) nodular goiter with involution or hyperplasia (non-toxic adenoma and toxic adenoma) and (3) diffuse goiter with hyperplasia (exophthalmic or true Graves' disease).

Rienhoff, Boyd and others considered goiter as being a continuous disease, the classification given above being merely stages of the same disease; the difference in the clinical picture being due to variations in the etiological agent or agents whatever they may be. The gland goes through many periods of hyperplasia and involution. The simple colloid or diffuse non-toxic goiter is a quiescent goiter in which there has been a mild stimulation with sufficient iodine present in the body. The various types of nodular goiter represent glands which have suffered many attacks of excessive stimulation and in which there have been many cycles of hyperplasia and involution. These glands will have areas of both hyperplasia and involution at the same time. It is doubted if the toxic agent causing symptoms arises from the large adenoma or the nodule seen in the so-called nodular toxic goiter.

* From the Department of Radiology of the Hospital of the University of Pennsylvania, Philadelphia.

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Rather it is felt that there are minute islands of hyperplasia throughout the other parts of the gland which give rise to the symptoms. The diffuse toxic gland or exophthalmic goiter is the result of a severe stimulation associated with a marked deficiency of iodine which results in hyperplasia of this gland without any evidence of involution. Hellwig[16] has recently reported the development of thyroid nodules in rats fed upon a calcium-rich diet. The diet causes the development of diffuse hyperplasia in the majority of animals. This report lends support to the idea that nodule formation and diffuse hyperplasia arise as the result of the same stimulating agent. Boyd[5] states that in a small number, less than 20 per cent of all adenomatous goiters, the adenoma appears to be a true neoplasm and therefore entirely different in origin.

The etiological agent of thyrotoxicosis is unknown. Apparently some irritant, bacterial or otherwise, acts continually upon the thyroid. Joll[19] gives the predisposing etiological factors in the production of exophthalmic goiter as: (1) heredity, (2) influence of the vegetative system, (3) influence of adrenal gland and (4) influence of the thymus gland. Crile contends that the disease is due fundamentally to a disorder of the adrenals. Marine[20] believes that Graves' disease is not a disease of the thyroid gland but that the primary and fundamental disturbance lies elsewhere, probably in a deficiency of some function of the suprarenal cortex and sex gland, which has to do with regulatory control of oxidation processes in the various tissues. Graves' disease appears to be associated with a loss of control of these oxidation processes and as a result of this there is excessive production by the thyroid of its very powerful activator of oxidation, thyrotoxin.

Recent advances in our knowledge of the thyrotropic hormone secreted by the anterior pituitary point toward this substance as being a very important factor in the development of hyperthyroidism, although the exact mechanism by which this substance acts is not yet generally agreed upon.

III. CLINICAL ASPECTS

Boyd[5] gives an excellent summary of the clinical picture in thyrotoxicosis:

> The four cardinal symptoms are enlargement of the thyroid, exophthalmos, tachycardia and excitability of the nervous system evidenced by tremors, etc. In addition, the skin is moist and readily becomes flushed, the patient is very excitable and irritable, palpitation, diarrhea and vomiting occur, and peculiar eye symptoms are frequent. Loss of weight is a constant factor.
>
> Perhaps the most important change is the enormously increased body metabolism as indicated by calorimetric observations. It is as if some blast were blowing on the furnace of the body, fanning it into a condition of furious activity. There is no other disease condition in which a comparable increase occurs. As a result of the rapid nitrogen metabolism it is but natural that the patient should waste away as if being burnt up. On the other hand, carbohydrate metabolism is so interfered with that the sugar tolerance is lowered, the blood sugar is above normal, and glycosuria is apt to occur. This may be due to the inhibitory influence which the thyroid is known to exert on the pancreas, or possibly to the heightened activity of the sympathetics interfering with the storage of glycogen in the liver.
>
> The course of the disease varies. It may be of an acute and fulminating type, the patient dying of the disease itself, with symptoms of acute hyperthyroidism, cardiac dilatation, wasting and exhaustion. Such cases accord with the classical picture described by Graves. Other cases pursue a less violent course, and are marked by a series of remissions and exacerbations, the histological counterpart of which is involution and hyperplasia. Finally there are still milder examples of hyperthyroidism which differs from acute Graves' disease in degree rather than in any essential qualitative manner. In these cases adenomatous nodules are very apt to develop as the result of involution, and such cases have been classed as toxic adenomas by Plummer and his followers. Closer investigation has shown that these cases do not differ from true exophthalmic goiter in any essential detail, either clini-

cally, histologically or in their response to iodine.

The disease is more or less self-limited. The fire burns itself out, the thyroid breaks down under the constant stimulation, degenerative changes follow, and a partial condition of myxedema or thyroid insufficiency may develop. By the time the thyroid has ceased hyperfunctioning, many of the vital organs, particularly the heart, have been permanently damaged, and the patient is apt to be permanently incapacitated.

Joll[19] has pointed out the differential diagnostic symptoms between the two types of thyrotoxicosis in a table as follows:

Primary Toxic (Exophthalmic or Toxic Diffuse) Goiter	*Secondary Toxic (Toxic Nodular) Goiter*
1. Onset may be acute and is often rapid.	1. Onset generally very insidious. Acute form very rare, and almost exclusively due to excessive iodine medication.
2. Young adults, usually previously goiter-free, affected.	2. Middle aged patients often goiter-bearers of long standing, affected.
3. Exophthalmos common and often severe.	3. Exophthalmos rare and usually absent.
4. Nervous phenomena may be very prominent and often dominate the case.	4. Nervous phenomena are slight or absent.
5. Myocardial and vascular lesions may be inconspicuous until late stages.	5. Myocardial and vascular degeneration are usually prominent and early features.
6. Metabolic disorders are common. B.M.R. may be higher than 100 per cent.	6. Metabolic disorders less common. B.M.R. rarely reaches 50 per cent.
7. Gastro-intestinal and other crises not uncommon.	7. Crises very rare.
8. Goiter usually diffuse, hyperplastic and symmetrical, rarely very large.	8. Goiter nodular and may be enormous. Exceptionally goiter may be diffuse and parenchymatous or colloid in type.
9. Secondary anemia rare.	9. Secondary anemia not uncommon.
10. Iodine medication often dramatic in its effect in reducing activity of symptoms.	10. Iodine medication, though often beneficial, not so striking in effect.
11. May rapidly progress to a fatal termination in delirium and coma.	11. The disease is a chronic one, and death, when due to thyrotoxicosis, is the result of the myocardial and vascular lesion.
12. Operative risk appreciable.	12. Operative risk less than in primary.
13. Operative curves about 90 per cent.	13. Operative cures approach 100 per cent.
14. Recurrences 6.5 per cent.	14. Recurrences 0.1 per cent.

As was discussed in the previous section, it is our belief that diffuse toxic and nodular thyroid disease have the same underlying etiology. Therefore, the primary toxic disease, as described by Joll, is the acute, rapidly progressive and the secondary toxic goiter is the type with many exacerbations and remissions.

Recently Rose, Rose and Pendergrass[39] classified the clinical types of childhood thyrotoxicosis. Because of the value of radiation therapy in children, their description will be given in detail:

Three distinct clinical types of hyperthyroidism in children have been observed in the Philadelphia region. There is, first, a frank type which may be called primary in that the appearance of the thyroid enlargement is roughly coincidental with the onset of subjective symptoms. The degree of enlargement is not usually great, but the gland may be quite firm, with occasionally a roughly granular or 'pebbly' feel to the surface. Frequently, however, the degree of enlargement is very slight and the gland quite soft in consistency. The patients in this group present a clinical picture quite comparable to that of the adult form of primary toxic diffuse goiter, except that visceral complications (cardiac, hepatic, etc.,) are much less frequent. Exophthalmos is common.

The second variety of the disease resembles that just mentioned in all respects except that the symptoms appear as secondary phenomena in patients with previously existing non-toxic goiters, either soft or firm in consistency. The

presence of palpable nodules (frequently called 'adenomata' without justification), in the toxic goiters of children or adolescents, is rare in this region.

The third type may appear in children with or without pre-existing goiter. The thyroid gland is seldom markedly enlarged, and is usually soft or elastic in consistency. The clinical picture is that of the 'forme fruste':—most of the characteristic symptoms of the disease are usually present, but often in miniature or with marked variation in intensity from time to time. The basal metabolic rate is usually elevated only moderately or slightly, and these patients pass through prolonged periods of spontaneous remission. Indeed, permanent spontaneous remission is commoner than in the other two groups of patients. Exophthalmos is seldom seen. Thyroid enlargement may persist after the disappearance of all symptoms. Subjective nervousness and tachycardia, the commonest symptoms in this group, may persist for some time after the basal rate has returned to normal levels. In some cases it is impossible, even after prolonged observation, to be certain whether the picture is that of a mild hyperthyroidism or of a non-toxic goiter with coincidental nervous symptoms and a borderline elevation of the metabolic rate. Mitral stenosis, congenital heart lesions, and paroxysmal tachycardia are occasionally mistaken for hyperthyroidism.

The syndrome known as 'sympathetic imbalance,' or 'hyperthyroidism without increased basal metabolism,' occasionally offers some diagnostic difficulty in children and adolescents, especially when there co-exists a non-toxic goiter. The principal point in differentiation from true hyperthyroidism is that the basal metabolism is never consistently elevated. The histologic picture of the thyroid is not that of toxicity. Specific therapy directed against the thyroid is ineffective, although iodine is said to have caused improvement in a few cases.

IV. CONSIDERATION OF TREATMENTS NOW IN USE

In view of the lack of knowledge and understanding of the physiology of the thyroid as well as a paucity of information as to the thyrotoxic states, it is obvious that any therapeutic approach to the problem will be empirical.

Rose[31] very concisely states the difficulties in evaluating any type of treatment instituted for thyrotoxicosis as (1) lack of exact knowledge of the actual cause of hyperthyroidism and its relation to the sympathetic nervous system and other endocrine glands, (2) the notorious variability of its spontaneous remissions, and even permanent cessation, (3) the confusing temporary effect of rest, hyperalimentation and sedative medication which are often component parts of other methods of treatment, (4) the effects of iodine therapy which are not yet completely understood, (5) the difficulty of following patients over a sufficient period of time to determine the permanence of alleged cures and the paucity of reliable statistics on this phase of treatment.

According to him any plan of treatment should fulfill the following prerequisites: (1) it should entail a minimum amount of immediate risk, (2) it should produce a maximum of residual results, (3) it should involve the least possible loss of time and earning power during its application, (4) it should be followed by a minimal number of recurrences, (5) its effect should be apparent in the shortest possible time, (6) it should be effective in checking permanently the complications of hyperthyroidism, particularly heart disease, and (7) it should be available to the average majority as well as to the expert few.

There are three plans of treatment which may be used in the care of these patients. Many times a combination of all three is necessary. The first or medical plan has been designated that of skillful neglect. For the great majority of thyrotoxic patients it is wholly inadequate.

The second or surgical treatment is the one of choice of many leading surgical clinics. The good statistical reports from these clinics justify this procedure. However, there is some difference of opinion regarding its efficacy in all cases of exophthalmic goiter. The not infrequent cases of postoperative recurrence lend a basis for this difference of opinion.

Crile[11] reported the results of 20,000 cases operated upon for hyperthyroidism in whom 80.9 per cent were in good condition after one year; 17.1 per cent were in fair condition and 4.4 per cent showed recurrence. The mortality rate was 0.5 per cent. The figures here quoted are probably the best of the statistics from surgical clinics. It must be remembered that the very low mortality rate and very high percentage of favorable results reported by a few very skillful operators working in well-organized clinics by no means results from the work of the rank and file of men doing goiter operations.

Clarke and Black[9] made a very interesting study of 76 out of 181 postoperative cases. Their data were obtained two and a half years postoperatively and the collection and correlation of it was done by someone other than the surgeon who performed the operation. They were careful to avoid pointed questions and the use of suggestion. Basal metabolic rates and physical examinations were done. They believe that in many cases the patient will not reveal his true condition to the surgeon who operated. Considering the symptoms most frequently complained of, i.e., weakness, nervousness and palpitation, 50 per cent were unable to regain their usual health. This, in association with unusual sensitiveness to cold, edema and hoarseness pointed to myxedema. Forty-two per cent showed no change in weight after operation (70 per cent had lost weight before operation). In 46 per cent there was no improvement in the pulse rate. The most critical test of results is the general physical status of the patient a few years after operation. With this criterion in mind, 16 per cent were entirely cured, 40 per cent moderately improved, 34 per cent showed some improvement and in 10 per cent there was a definite return of toxicity. In other words, 56 per cent obtained sufficient relief to be classified as average normal healthy persons and in 44 per cent there was either a persistence of symptoms or a recurrence so that they could not be classified as normal healthy persons. These authors conclude that the disease is constitutional; that removing the gland is only removing a link in the train of symptoms, thus changing the condition from a toxic hyperthyroidism to a less bothersome and less dangerous hyperthyroidism. The removal of the gland is merely substitutional therapy; it alleviates the underlying condition but does not alter it.

The third method of treatment is irradiation. During the past thirty years there has been an increasing number of reports, both in American and in foreign literature, concerning this form of therapy. Many of these reports are lacking in scientific value; furthermore, there is no uniformity in terminology in reporting the results. There have been, however, a few carefully checked studies which point to the value of this therapeutic agent.

V. IRRADIATION

(*a*) *History*. The first American reference to this form of therapy was by Williams[42] in his book on "The Roentgen Ray in Medicine and Surgery" published in 1901. Blalock[3] treated a case of goiter successfully with six exposures and reported the case in 1903. Spring[35] reported improvement in 3 cases of goiter in 1903. In 1902 Campbell[7] reported improvement in the goiter of a patient treated for acne. Pusey and Caldwell,[27] in their text published in 1903, reported some good results and some poor ones.

(*b*) *Literature*. Pfahler and his associates have made more contributions to the American radiological literature upon this subject than any other group. His first report was in 1904 and this was followed by reports in 1906, 1908, 1916, 1930 and 1932 as well as other minor articles on the subject. In 1916, Pfahler and Zulick[26] presented a masterly article which included a review of the literature and said, "It is utterly impossible to draw conclusions from any collection of statistics upon this subject because the cases reported show such a variation and such indefinite technique that the reduction of the statistics to percentage would give us nothing accurate by which we could

judge future results. One must draw conclusions as to the value of the treatment more from the individual opinion of competent observers than from any mathematical calculations."

Their conclusions were that (1) all cases of hyperthyroidism should be given at least one roentgen treatment and wait one month before operation, (2) treatment should be directed toward the thymus as well as toward the thyroid, (3) the increase in weight and decrease in pulse are the first improvements noted, (4) treatments should not be prolonged over too great a period and (5) the goiter and exophthalmos are the last signs to show improvement and many times show no change.

In 1930, Pfahler and Vastine[25] reported on the results of roentgen therapy in 400 cases, in which 86 per cent of 235 were cured or markedly improved. Of the patients seen during the first three months of the disease, 96 per cent were cured; 8 per cent of the patients treated later came to operation and 8 per cent of all under treatment were postoperative recurrence. In this series they reported 91 per cent of the patients with toxic adenoma as improved.

In 1932, Pfahler[24] again made a report on this form of therapy in which it is recommended that all patients with hyperthyroidism should be given a preliminary trial of radiation therapy unless symptoms are so acute that delay is not advisable. The technique of treatment is described as being low voltage (135 kv. (peak)) giving 40 per cent S.E.D. to each of four fields as one series and repeating the series in three to four weeks. Usually five to eight series are necessary. If there is no improvement after three to four weeks then surgery is recommended. Treatment is stopped when the basal metabolic rate reaches +10 or +15 per cent. Toxic adenoma is reduced in size and the symptoms are alleviated.

In 1923, Groover, Christie and Merritt[14] enumerated the reasons advanced by surgeons for not accepting irradiation as a means of treating toxic thyroids as: (1) it has not been proved that roentgen rays produce a permanent cure, (2) the time necessary for roentgen treatment increases the opportunity for cardiovascular and visceral changes to occur, and certain patients die of hyperthyroidism while taking the treatments, (3) subsequent operation upon the gland is rendered more difficult because of adhesions between muscles, capsule and gland, (4) the function of the gland may be so reduced that hypothyroidism will result.

They stress the importance of the general management of these patients which includes rest, diet, cardiac, nervous and gastrointestinal supervision. They conclude that (1) a comparison of results shows that surgery and irradiation are probably equal in percentage of cures, (2) patients with hyperthyroidism should have thyroidectomy only after a trial with irradiation, (3) the general management of patients with hyperthyroidism is of great importance whether ultimate treatment is to be roentgen irradiation or surgery.

In 1925, Christie,[8] in a study of surgical statistics collected from various clinics, concluded that this procedure cured 60 per cent of thyrotoxic patients and afforded relief to 15 per cent more and that the mortality rate was 1.5 to 4 per cent. He concluded that roentgen irradiation should be tried in all cases preliminary to surgery.

In 1929, Groover, Christie, et al.[15] reported the results of irradiation in 305 cases as follows: 88.8 per cent cured, 8 per cent improved, 2.6 per cent unimproved. The average number of treatments was 6.6. A case was considered cured when there was a disappearance of signs and symptoms of thyroid intoxication with a return to normal of the basal metabolic rate, but this cure did not necessarily imply a complete disappearance of some by-effects of the disease. The factors contributory to failure were given as (*a*) overwhelming toxicity, (*b*) serious cardiovascular or other visceral changes and (*c*) non-cooperation on the part of the patient or attending physician.

Soiland, Costolow and Meland[33] collected the results of irradiation of 3,100 cases administered by 20 different radiologists and their figures showed 73 per cent were clinically well, 16 per cent were improved and 11 per cent unimproved.

Menville[22] collected reports from 200 radiologists regarding the results in 10,541 cases treated by this form of therapy: 66.2 per cent were cured, 21.07 per cent improved and 12.4 per cent were failures.

Meyer[23] summarized ten years' experience by concluding that (1) adolescent goiters responded well, (2) patients on iodine therapy

were not so responsive and (3) 84 per cent of patients with Graves' disease improved, of which 66 per cent were completely symptom-free.

Barclay and Fellows[1] reported that of 300 cases 63.3 per cent were cured, 25 per cent improved, 5 per cent not improved and 6.6 per cent were lost sight of.

Stevens[36,37] considered that irradiation is indicated in any case of hyperthyroidism, especially in a case with a high basal metabolic rate or one with a low basal metabolic rate which is rapidly rising. The only contraindication is a goiter presenting pressure symptoms. In discussing the results in 325 cases, he stated that 90 per cent were cured as indicated by return to normal pulse and basal metabolic rate and the regaining of weight loss.

Jenkinson[18] believed that most, if not all, cases of exophthalmic goiter can be cured by roentgen irradiation.

Remer and Belden[29] recommended irradiation for toxic diffuse goiter and gave the order of improvement of symptoms as (1) improvement in nervousness, (2) diminution in pulse rate, (3) goiter and exophthalmos are the last symptoms to disappear. They believed that if there was no improvement in four treatments, surgery was indicated.

In discussing the use of radium in the treatment of this symptom-complex, Ginsburg[13] believed this type of irradiation to be indicated in (*a*) borderline cases, (*b*) mild or larval early cases, (*c*) cases with slight thyroid enlargement, (*d*) average case without compression, (*e*) postoperative persistent or recurrent cases, (*f*) very severe cases without compression in which operation is refused, (*g*) poor operative risks. Surgery is indicated in (*a*) cases refractory to judicious and efficient radium therapy, (*b*) cases with compression phenomena, (*c*) severe cases demanding quick economic restoration, (*d*) cases with large, long-standing adenomatous goiter demanding cosmetic results.

Quigley[28] believed that the results with radium compared favorably with those of surgery in 70 per cent of cases and that those not responding to radium would respond to surgery, and vice versa.

Williams[41] gave a statistical report of 200 cases treated with roentgen irradiation: 80.5 per cent were cured and 13.5 per cent definitely improved, 4 per cent recurred after one year.

Holmes et al.,[17] after a very critical and extensive study of the use of radiation therapy in the thyrotoxic condition at Massachusetts General Hospital where one-third of the cases showed no improvement and two-thirds showed improvement ranging from a mild to complete cure, concluded that at present, iodinization followed by subtotal thyroidectomy while the basal metabolism is normal, is the best program for the treatment of exophthalmic goiter that has yet been advanced. Roentgen irradiation will still have its place in patients in whom, for any reason, operation is undesirable or who refuse operation.

Richter[30] concluded that radiological literature relating to the treatment of thyrotoxicosis is extremely meager and adequately controlled objective data on which the student may base an opinion are lacking. Even on the basis of this inadequate study, from 20 to 50 per cent of failures are commonly admitted. Very mild, early, adolescent cases and patients with associated lesions incompatible with a reasonable life expectancy may advantageously be given radiotherapy. Radiotherapy offers no advantages over a short course of iodine as a preparatory method of treatment. He maintained that patients usually reported as improved upon a basis of reduction of basal rate should be classed as failures. He objected to the time element in using roentgen treatment.

Joll[19] evaluated the use of irradiation as follows:

> Although it is probably true that improvement occurs in a large percentage of early cases of thyrotoxicosis treated by x-ray, how much of this improvement is due to the natural course of the disease and how much from the treatment is difficult to determine. The wide variation in the interval before the patient begins to improve under x-ray treatment is in sharp contrast with the rapid improvement which follows surgical procedures, suggesting that the x-ray is not the only factor operative in bringing about the amelioration in the patient's condition. The mortality among patients under irradiation treatment, or within a few months of its cessation, is by no means negligible, and must usually be attributed to thyrotoxicosis itself, though the possibility of aggravation by the treatment must not be overlooked. The chief indication for roentgen therapy is in early cases associated with great restlessness and irritability and a large goiter.

Solomon and Gibert[34] reported improvement in 92 per cent of 48 severe cases of Basedow's

disease treated by roentgen irradiation. Their indications for radiation treatment are (*a*) in slight cases iodine therapy is indicated first, and if this fails give roentgen therapy, (*b*) in pronounced Basedow's syndrome (either in intensity or of long standing) roentgen therapy should be used, (*c*) in cases in which technically correct roentgen therapy has failed, operative interference is indicated. They emphasize the importance of accurate measurement of dosage as well as the necessity for treatment to be extended over three months before failure is conceded.

In the treatment of 43 cases of Basedow's disease by radium irradiation, Butler[6] reported cures in 62.7 per cent. With the heavier filtration now in use he encountered no unpleasant skin effects.

Bardachzi[2] concludes that the permanent favorable effects of roentgen therapy in complete Basedow's disease show that this harmless treatment should be used first in all such cases; if improvement does not occur within two to three months, operation should be done; where operation is refused or the operative risk too great, roentgen irradiation should be continued.

(*c*) *Comment on Reports.* In considering these few conflicting reports which have been quoted, and they could be multiplied many times over, one is impressed with the fact that there must be a middle ground in which irradiation has a place of value in the care of patients suffering from thyrotoxicosis.

The rapidly advancing strides in the technique of irradiation should be kept in mind by anyone trying to compare surgery and irradiation. The futility of attempting to draw conclusions from results of treatment given ten years or even five years ago will be clearly brought out later in this paper. Also, there is the untenable position of dogmatically drawing conclusions about the efficacy of surgery based upon the results of a few master surgeons. The critical judgment of surgical writers upon this subject is at once open to question when one sees them make statements regarding the danger of roentgen burns and of the formation of adhesions which increase the surgical difficulties of subsequent operations. The former "straw man" has been a thing of the past for many years except as a purely accidental occurrence, such as is comparable to the leaving of a sponge or instrument in the abdomen of a patient. The latter has been proved to be untrue over and over again.

On the other hand, such collected reports as Menville and others have accumulated have no scientific value whatever. There can be no uniformity in interpretation of such terms as cures, improvements, etc., nor can the accuracy of the observations be relied upon. So in an effort to arrive at some more tenable conclusions regarding radiation therapy in thyrotoxicosis, this study of the patients treated at the University Hospital was made.

(*d*) *Experimental.* It has long been known that the normal thyroid gland is very resistant to radiation. Colwell and Russ,[10] in 1915, quoted Rave who noted the almost complete lack of recognizable effect resulting from the exposure of the thyroid to roentgen radiation. This conclusion was reached following investigation with irradiation of thyroid glands of mice, rats, rabbits, guinea pigs and dogs.

Bower and Clark[4] implanted steel radium needles into the thyroids of dogs. These needles were left in place from two to thirteen and a half hours and the animals were killed from seven to 210 days later. They found a sharp line of demarcation between the destroyed (necrotic) and the normal gland, and they concluded: (*a*) the primary changes induced by radium in the thyroid were hemorrhage and necrosis; organization and healing were evidenced in the third week and completed about the twelfth, (*b*) the normal thyroid gland was distinctly resistant to the action of radium, the nuclear degenerative changes characteristic of irradiated malignant tissue were never seen, (*c*) no toxic symptoms of any sort were seen, (*d*) no changes were demonstrable in the parathyroids, (*e*) the apparent irresistance of thyroid tissue to irradiation would make it appear that implantation would be su-

perior to surface applications and that relatively large doses must be employed to insure extensive effect upon the gland.

Walters, Anson and Ivy,[39] employing the dosage usually used in treatment of hyperthyroidism gave radiation to dogs and the results were: (*a*) the histology of the normal thyroid of the dog was not materially changed by roentgen-ray dosage known to be of clinical value in 60 per cent of cases of hyperthyroidism; the tendency of the effect was toward hyperplasia, (*b*) the capsule of the thyroid was thickened only by an overdose which resulted in a skin ulcer, (*c*) the treatment used caused a definite hyperplasia of the parathyroid. In those dogs in which several months had elapsed after cessation of the treatment, an increase of connective tissue of the parathyroids occurred. A gradual slight decrease in blood calcium occurred in spite of the hyperplasia. These results indicate that the parathyroids are not affected by the dosage usually given for clinical purposes. The experimental literature surveyed by these authors indicates that normal thyroid tissue is resistant to irradiation.

The following year the same authors[40] attempted to prevent the hyperplasia of the thyroid gland in the opossum by roentgen irradiation. As the thyroid gland of the opossum will undergo hyperplasia when the animal is fed meat, these authors treated two groups of animals, using the same dosage usually employed in treating a patient. They irradiated one group which was fed meat and another group which was not given meat. They found that the hyperplasia resulting from the feeding of meat to the animals was definitely decreased but not entirely prevented by the roentgen dosage employed. They suggested the clinical use of the roentgen ray to prevent postoperative recurrence and as an adjunct to preliminary iodine medication.

Friedman and Blumgart[12] had an opportunity to study the effect of irradiation upon the human thyroid gland. Four of their cases were given large amounts of radiation in an effort to eliminate the thyroid function in patients suffering from chronic cardiac conditions. Two of the patients had had previous subtotal thyroidectomies. Doses two and three times the amount usually given to thyrotoxic patients had no influence upon the basal metabolic rate. Two patients were irradiated by the Coutard technique, 4,000 r without back-scattering using high voltage and heavy filtration. This amount of radiation had no effect upon the basal metabolic rate. Three months later total ablation was done and the pathological report was normal thyroid tissue. This would indicate that to destroy the function of normal thyroid gland, prohibitive dosage must be used.

VI. TECHNIQUE OF TREATMENT

The technique of treatment was varied at rather frequent intervals during the seven and a half years under consideration. At first, radium was used almost exclusively. It was applied in the form of a block or pack to ten to twelve small areas. The filtration was 1.5 mm. of brass plus 1 mm. of rubber and the distance was 0.5 cm. A series consisted of 100 mg-hr. to each of the small portals. Usually two series were given thirty days apart.

Later radium was used in the form of a large pack and was applied to each half of the gland as a series. The filtration was 4 mm. of lead and the distance 3 cm.

During the early part of the period a series of roentgen treatments consisted of the following factors: 135 kv. (peak); 5 mm. Al filtration; 4 min., through 4″×4″ portals to four different areas over the gland. This gave approximately 125 r and a series would be given at three-week intervals. Later the dosage was increased to about 250 r and given to the gland through one large portal.

The last year and a half the filtration was changed to 0.25 mm. Cu plus 1 mm. Al, and 400 r was given through one large portal to the gland.

At the present time (August, 1934) the routine procedure in the care of the thy-

rotoxic patient is as follows: first, a careful examination is made by the thyroid clinic. This includes a basal metabolism test and the usual physical examination. Second, a roentgenogram is taken of the chest. The purpose of this is to exclude a latent pulmonary tuberculosis, a substernal thyroid or a persistent thymus.

One of two general plans is followed. Most frequently the patient is given three series of treatments at intervals of three weeks, following which a basal metabolic reading and check-up by the thyroid clinic is done. The roentgen-ray factors are: 135 kv. (peak) (mechanical rectification); 5 ma.; 0.25 mm. Cu plus 1 Al filtration and 30 cm. distance. The factors produce a wave with the following characteristics: output 27.0 r per min.; half-value layer, 0.42 mm. Cu, effective wave length, 0.23Å; 400 r, measured in air, is given at one time and this constitutes one series. The portal used is 12×15 cm. and includes the anterior thyroid area and the cervical sympathetics (Fig. 1). The larynx is protected from direct irradiation. In the very occasional patient, this amount of irradiation will cause a reddening of the skin but this reaction is very transitory. The treatments are continued until the basal metabolic rate is between 0 and +10 per cent. As the rate subsides and approaches normal, the readings are made three or four weeks after each treatment.

The second technique used at times employs the following factors: 165 kv. (peak) (valve tube rectification with condensers, giving a ripplage of approximately 0.5 per cent per milliampere); 15 ma.; 0.5 Cu plus 1 Al filtration; and 50 cm. distance. The wave produced by these factors has the following characteristics; output 40.0 r per min.; half-value layer, 0.88 mm. Cu, effective wave length, 0.17 Å. The same portal is used when the lower voltage is employed; 200 r, measured in air, is given every other day for three days, and 600 r constitutes a series. A basal metabolic reading is taken in one month and further treatment depends upon the results obtained. This technique is frequently used in those cases in which the low voltage

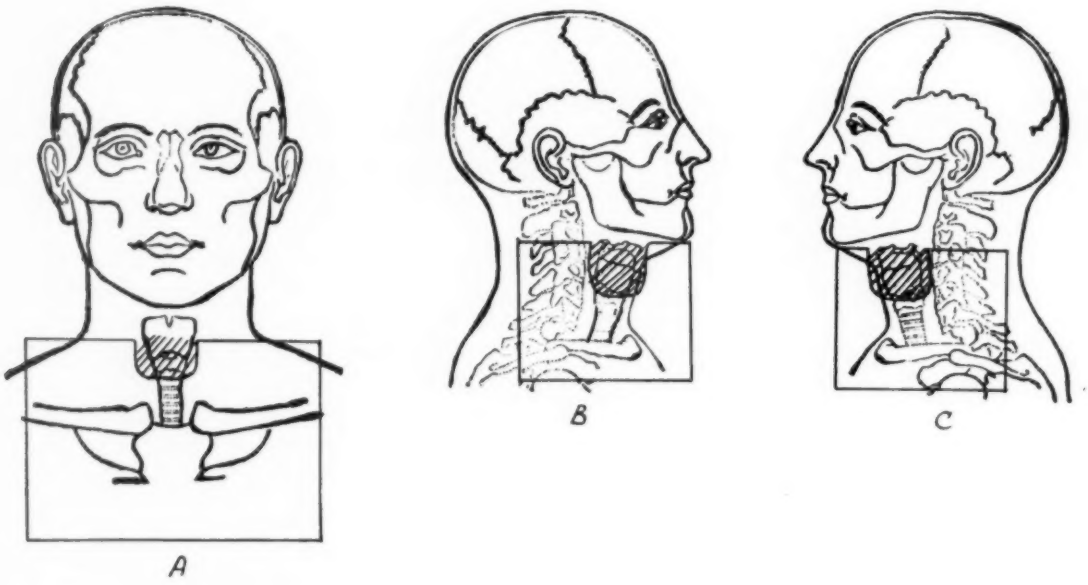


Fig. 1. *A* represents the portal most commonly used at present. *B* and *C* represent portals made use of only occasionally.

has been ineffective. It appears that the change in wave length has a beneficial effect in a certain number of cases.

Radium is used only in those patients too ill to be transported to the radiological department. When it is used, the filtration is 2 mm. of platinum or equivalent; the distance 4 cm., and 1,000 mg-hr. is given to each lateral area. One month is allowed to elapse before additional treatment is given.

In the use of roentgen irradiation, the importance of accurate calibration in roentgens must be stressed. The r output of our equipment is checked each month, or oftener if a new tube is put into use. It is only in this manner than an accurate knowledge of dosage can be recorded.

In cases of hypertension associated with hyperthyroidism, an additional field over the dorsal and lower cervical sympathetics is included in the series. It has been shown experimentally that irradiation will inhibit the transmission of impulses along the sympathetics.

The postoperative cases which do not respond to a moderate amount of irradiation are given treatment over the pituitary gland in an effort to diminish the amount of thyrotropic pituitary hormone. In a few cases this has been helpful.

Iodine is not given to the patients receiving radiation therapy. To do so would confuse the evaluation of the results of treatment and would rob the patient of the optimum advantages of preoperative iodine administration should surgery be necessary.

VII. STATISTICAL REPORT OF RESULTS IN OUR CASES

From January 1, 1926, to July 1, 1933, 350 patients were given radiation therapy for toxic goiter at the University Hospital. Of this number only 244 could be used for statistical study. The females outnumbered the males about 4 to 1 (195 females compared to 49 males). The majority of the patients were in the third, fourth or fifth decade of life.

AGE		NATIONALITY	
10–20	27	American	208
20–30	61	Austrian	2
30–40	69	Jewish	14
40–50	51	Irish	1
50–60	20	Colored	9
Over 60	15	Russian	4
Not stated	1	Italian	1
	244	Not stated	5
			244

MARITAL STATE

Single	73
Married	136
Widowed	25
Not stated	10
	244

The duration of symptoms ranged from a few weeks to two years or over. The greatest number had been ill less than six months.

DURATION OF SYMPTOMS

Less than 6 months	72
6 months to 1 year	43
1 to 2 years	46
2 years or over	65
Duration unknown	18
	244

Diffuse toxic goiter was the most common type. There were 41 cases treated which had recurred after surgical procedure:

TYPE OF GOITER

Diffuse toxic	179
Nodular toxic	21
Recurrent diffuse toxic	39
Recurrent nodular toxic	2
Unclassified	3
	244

Adjuvant treatment was recorded as having been given in 65 cases. This usually consisted in the administration of iodine. It is felt, however, that iodine should be omitted while irradiation is being given. The records contained mention of the presence of foci of infection as existing in 44 out of 244 patients. The most common foci mentioned were diseased teeth and tonsils.

A study of the duration of the follow-up period showed that over one-half of the patients had been followed twelve months or less:

DURATION OF FOLLOW-UP PERIOD

Less than 6 months	101
6 to 12 months	53
12 to 18 months	30
18 to 24 months	11
24 to 36 months	13
36 to 48 months	11
48 to 60 months	9
Over 5 years	16
	244

In order to evaluate the results a classification table was devised by which the patients could be grouped:

CLASSIFICATION

A. Completely well with the patient free of any residual symptoms.

B. B1. Much improved. Completely relieved but with slight residual findings such as elevated basal rate or a slightly rapid pulse.

B2. Moderate improvement. Each case to be evaluated individually.

C. Those patients who did not complete the proposed treatment.

D. D1. Treated as poor surgical risks preliminary to surgery but who did not come to surgery.

D2. Same as above but those who did come to surgery.

E. Failures.

E1. Complete failures.

E2. Temporary improvement but with ultimate surgery.

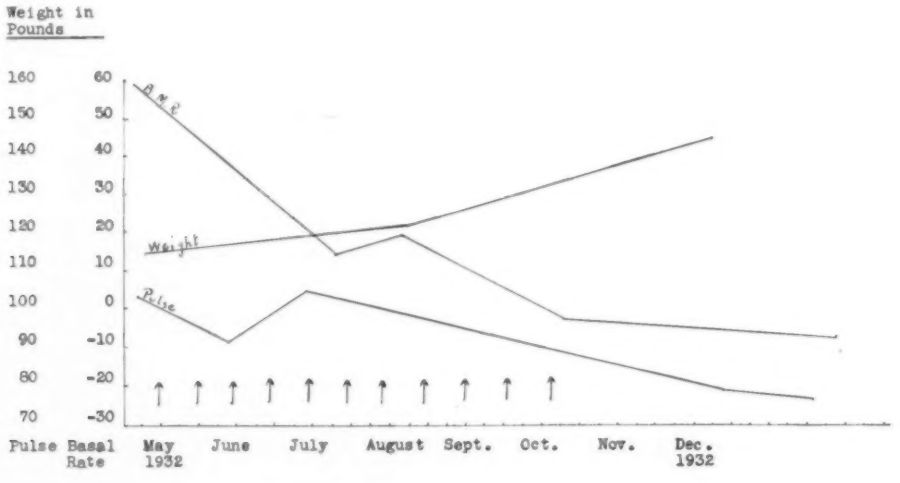
In this table we considered it proper to consider all patients who fell in Groups A, B1, B2 and D2 as being good results. According to this classification it was found that good results were obtained in 69.9 per cent of all cases treated from 1926 to 1933. (The cases in Group C were not included in the calculation of percentages.) The interesting part of the analysis of the results is to see the marked improvement during the latter part of the period as the technique became more efficient. During the years 1926 to 1928, good results were obtained in only 50 per cent of cases treated; from 1929 to 1931 the percentage went to 68, while in 1932 and 1933 good results were obtained in 90 per cent of cases.

Charts I and II graphically depict the course of 2 cases in which excellent results were obtained.

RESULTS

All Cases		*Recurrent Cases*		*Nodular Cases*	
A	78	A	12	A	5
B1	26	B1	2	B1	0
B2	24	B2	7	B2	2
C	51	C	10	C	4
D1	3	D1	0	D1	3
D2	7	D2	2	D2	2
E1	49	E1	8	E1	3
E2	6	E2	0	E2	2
	244		41		21

It will be seen that 74 per cent of recurrent cases were distinctly benefited and that good results were obtained in 53 per cent of the nodular toxic group.



Each arrow indicates one x-ray series.

CHART I

No conclusions could be drawn between the results obtained and the number of series of treatments given. Just as many series of treatments were given to the cases in which no improvement was obtained as in those cases where the results were satisfactory. As a rule two series of radium treatment and ten series of roentgen treatment were given.

NUMBER OF SERIES OF TREATMENTS IN EACH GROUP

Results	*Series of Radium*	*Series of X-ray*
A	1.6	10.08
B1	2	11.4
B2	2	12.1
C	1	3.2
D1	1	12.5 (2 cases)
D2	1.6 (5 cases)	11.4 (5 cases)
E1	1.5	9.09
E2	2.6 (4 cases)	11.5 (2 cases)

A study was made of the relationship between the duration of symptoms and the results obtained. There appeared to be no significant relationship in this series. The duration of symptoms was not noted in 21 cases.

RELATIONSHIP OF DURATION WITH RESULTS

	A	B1	B2	C	D1	D2	E1	E2
Less than 3 months	9	3	0	3	0	0	8	1
3 to 6 months	20	5	3	10	0	1	9	4
6 to 9 months	10	3	0	3	0	1	6	2
9 to 12 months	4	1	4	6	1	0	3	1
12 to 18 months	7	1	2	5	0	1	2	0
18 to 24 months	7	5	2	4	2	3	4	1
24 to 26 months	8	2	6	9	0	0	6	0
Over 3 years	8	7	1	5	0	4	6	0

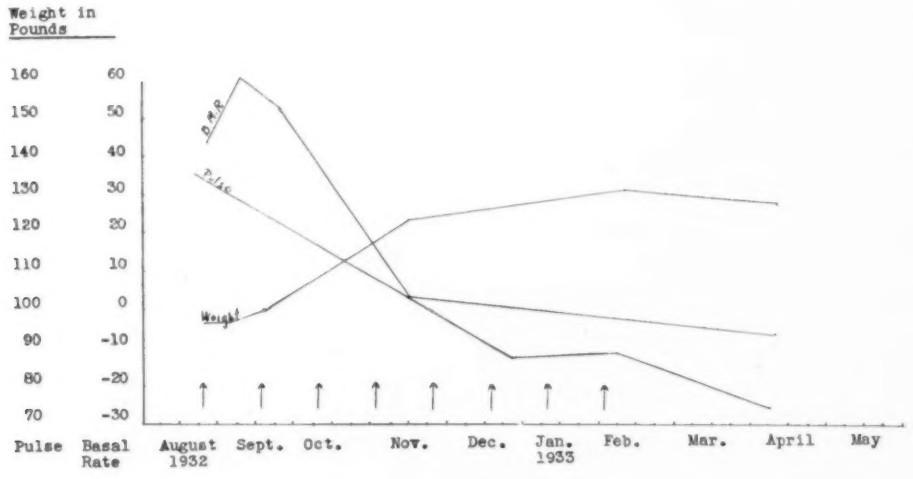
During the period of this study there was no mortality while treatments were being given. The only death in a thyrotoxic patient under the care of the radiological department occurred after the time limit of this study. This mortality was in an adolescent girl whose cardiac condition was not kept under sufficiently careful observation, and the case is reported in detail elsewhere by Rose, Rose and Pendergrass.[32]

The patients were grouped in age periods to show the results obtained. There was not enough variation in the percentage of good results in the different ages to indicate that the age of the patient has any bearing upon the response to be expected.

RESULTS IN RELATION TO AGE GROUPS

	A	B1	B2	C	D1	D2	E1	E2	Percentage of Good Results Omit c Group: A B1 B2 D2
10–20	8	4	3	2	0	1	6	1	16	69
20–30	20	3	4	21	0	1	15	3	28	60
30–40	23	8	5	13	0	0	15	1	36	69
40–50	19	6	3	7	0	3	10	0	31	76
50–60	5	2	5	4	1	2	2	2	14	73
over 60	2	3	4	4	2	0	1	0	9	75
Unknown	1	0	0	0	0	0	0	0	0	
Total	78	26	24	51	3	7	49	7		

A table was made to illustrate the relationship between the results and the duration of the follow-up. It was noted



Each arrow indicates one x-ray series.

CHART II

that 74 per cent of cases showing good results were followed two years or less.

RESULTS IN RELATION TO FOLLOW-UP PERIOD

	A	BI	B2	C	DI	D2	EI	E2	A BI B2 D2
Less than 6 mo. 101	13	6	5	45	1	3	26	2	27
6–12 mo. 53	18	9	11	4	1	1	8	1	39
12–18 mo. 30	14	4	5	1	1	0	4	1	23
18–24 mo. 11	7	2	1	0	0	1	0	0	11
24–36 mo. 13	8	1	1	1	0	0	2	0	10
36–48 mo. 11	5	1	0	0	0	0	3	2	6
48–60 mo. 9	6	1	0	0	0	0	2	0	7
Over 5 yr. 16	7	2	1	0	0	2	4	0	12
Total	78	26	24	51	3	7	49	6	135

VIII. DISCUSSION AND SUMMARY OF RESULTS

It has been observed that the patient whose major symptom is nervousness, who has a small soft goiter, and who has been ill six months or less has the best prognosis for relief by irradiation. In these patients the economic saving from this form of therapy is considerable. Many of them continue with their occupation. Even in those cases in which a rest period of two to four weeks is desirable at the beginning of the treatment, the financial outlay is still much less than when surgery is necessary.

There are certain patients who have a dread of surgery and will not permit operative procedure, regardless of how desirable it may be. To these individuals, irradiation offers some hope of relief.

It has come to be the feeling in this hospital that all children with thyrotoxicosis should be given irradiation before surgery is considered. Rose, Rose and Pendergrass[32] concluded that adequate irradiation of the thyroid gland in this disease is followed sufficiently often by satisfactory permanent remission to justify a carefully controlled trial provided efficient apparatus is available. If definite improvement does not appear within three months, or if a marked exacerbation of the disease appears at any time, irradiation should be stopped and preparation for thyroidectomy begun. By such a course the thyroid gland can be saved and this is very important to the adolescent whose endocrine glands are in the process of adjustment for adult life.

As with any form of therapy, there are disadvantages in the radiation treatment of hyperthyroidism. The treatment extends over some little time and there is always the possibility that very serious visceral changes will take place before the beneficial results become manifest. This possibility can be prevented by a careful selection of patients and by careful observation and check of the status of the disease while treatment is being given.

Roentgen sickness is encountered in the occasional case. This distressing symptom does not occur as frequently as when malignancy is being treated. As yet no preventive for radiation sickness has been found.

A temporary exacerbation of the symptoms of thyrotoxicosis can be expected for twenty-four to seventy-two hours after the first few treatments. This reaction is not serious and ordinarily subsides with rest and sedatives.

In the occasional patient, there is a slight to mild skin reaction in the area treated. This is never more than a first degree reaction and soon disappears. In the earlier period a very occasional case of telangiectasis was seen as a late result of treatment. This has not occurred since the use of higher filtration was instituted. The possibility of alopecia developing while the patient is under treatment must be kept in mind. Not infrequently this is a symptom of the disease and is never the result of irradiation if ordinary care is taken to protect the hair with lead rubber. It is customary to have the patient or responsible relative sign a release card which mentions the possibility of alopecia.

It must be remembered that hyperthyroidism is a disease characterized by spontaneous remission and exacerbation of symptoms. If a severe case is given treat-

ment during a period of rising toxicity, there is the possibility of unfortunate results. Such results bring unjustifiable criticism upon this form of therapy. It is considered advisable to refuse to treat such patients or to have a very clear understanding of the possibility with all concerned and especially with the referring physician. The extremely toxic patients are best treated in their rooms with small doses of radium.

There is also the possibility of depressing the thyroid activity to the point where myxedema develops. This occurs very infrequently and can be readily controlled by thyroid medication.

The size of the goiter is influenced little if any by irradiation. At times there is a demonstrable reduction in the size of the gland, but this is by no means the rule.

One may conclude from this study that with the present selection of cases, excellent results are being obtained, as evidenced by the 90 per cent of cases improved during the years 1932 and 1933. These latter cases have not been followed long enough for definite conclusions to be drawn.

It must be remembered when considering the statistics quoted above that there was a definite selection of cases and some of the good results during the latter period are probably due to a better recognition of the type of case amenable to irradiation.

The basis for selection of cases for irradiation is as follows:

1. Postoperative recurrences are treated without selection.
2. Patients in whom it is felt that roentgen irradiation offers a reasonable chance of cure without the necessity of operation. These are the patients in whom, if roentgen irradiation should be ineffective, the chances for surgical cure would not be materially impaired. This group of patients includes:
   a. Those with mild to moderate degrees of hyperthyroidism in whom the predominating symptom is nervousness, and in whom there are no evidences of visceral damage.
   b. Those with little or no loss in weight.
   c. Those with slight to moderate thyroid enlargement and in whom the goiter is not hard or nodular.
3. All children with toxic symptoms are treated, except those with nodular goiters.
4. Patients who are a poor operative risk and the irradiation is given as a preoperative procedure.
5. Those in whom surgery is definitely indicated but who refuse this form of therapy.

IX. CONCLUSIONS

1. The pathology, physiology and symptomatology of the thyrotoxic states have been briefly reviewed.

2. The present methods of treatment have been discussed, including a review of the English and American literature of radiation therapy.

3. An analysis of the cases treated at the Hospital of the University of Pennsylvania during the past seven and a half years has been given and from this analysis it is felt that in selected cases radiation therapy is eminently successful and, such being the case, this form of therapy has a definite place in the treatment of thyrotoxicosis.

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PLANIGRAPHY

II. MATHEMATICAL ANALYSES OF THE METHODS, DESCRIPTION OF APPARATUS, AND EXPERIMENTAL PROOF*†

By J. ROBERT ANDREWS, M.D., *and* ROBERT J. STAVA, B.S.
CLEVELAND, OHIO

IN THE first communication of one of the authors[1] on the subject of planigraphy, six methods for the solution of the problem presented in the roentgenographic projection of a true image of a plane section of a solid object were described. Before a planigraphic apparatus was constructed, however, it became necessary to analyze more critically the mathematical, physical and mechanical problems involved in the application of the planigraphic principle. As this analysis proceeded, it became evident that the claims which had been proposed by the originators of some of the methods could not be substantiated because it could not be proved that a true plane section would be projected by these methods. As this analysis proceeded, it also became evident that there were two methods whereby a practical solution of the problem could be attained and mathematical proof would demonstrate that a true plane section would be projected.

The analysis of one faulty and two correct methods will therefore be presented. The incorrect method is that of Vallebona, described by him as "stratigraphy" (method No. 4),[1] while the two correct methods are those of Ziedses des Plantes, described by him as "planigraphy" (method No. 5),[1] and Grossmann, described by him as "tomography" (method No. 6).[1]

Stratigraphy (Fig. 1).

Description. The roentgen tube and the cassette are fixed to the pendulum *AOB* so that they are perpendicular to the pendulum and parallel to each other. In operation the tube and cassette describe arcs. In position *A* the projection of the desired plane *LM* on the film is *XY* while in position *A'* the projection is *X'Y'*. If *XB* is drawn on the film in position *A'*, *X* will fall at *X''*

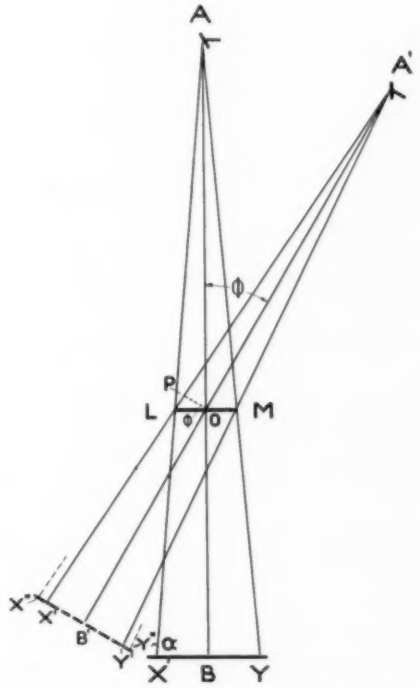

FIG. 1. Stratigraphy (for explanation of figure see text).

while the projection of *L* is *X'* and the error of the projection is *X'X''*. Therefore a true image of the plane *LM* is not obtained. The error, *X'X''*, is dependent upon the distance of the point, *L*, from *O*; the value of ϕ; and the distances, *AO* and *OB*.

Analysis:

From Figure 1

$$OP = LO \cos \phi$$

[1] Andrews, J. R. Planigraphy. 1. Introduction and history. Am. J. Roentgenol. & Rad. Therapy, 1936, *36*, 575–587.

* From the University Hospitals (Lakeside), Cleveland, Ohio.

† Part II of thesis submitted by Dr. Andrews to the Faculty of the Graduate School of Medicine of the University of Pennsylvania in partial fulfillment of the requirements for the degree of Doctor of Medical Science (D. Sc. (Med.)) for graduate work in radiology.

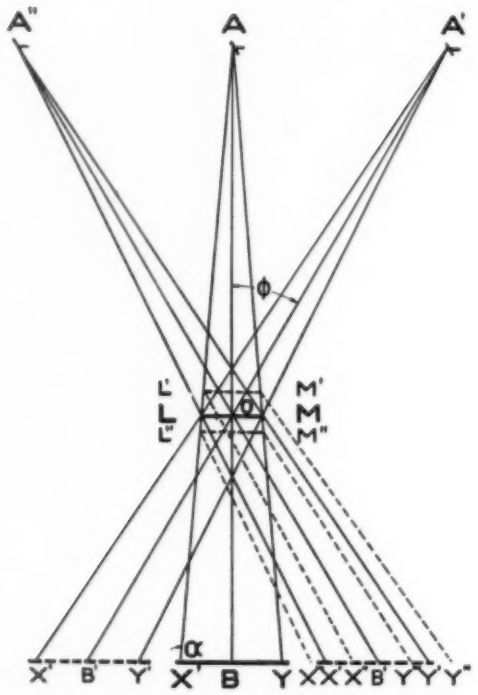

FIG. 2. Planigraphy (for explanation of figure see text).

and therefore

$$\frac{X'B'}{OP}=\frac{B'A'}{OA'}$$

or

$$(1)\qquad X'B'=\frac{OP\times B'A'}{OA'},$$

also

$$\frac{XB}{LO}=\frac{BA}{OA}$$

or

$$(2)\qquad XB=\frac{LO\times BA}{OA}.$$

Since $B'A'=BA$

and $OA'=OA$

substituting in (1)

$$X'B'=\frac{OP\times BA}{OA}.$$

Since OP is less than LO then $X'B'$ is less than XB in amount directly proportional to PO or LM. For the distance $X'B'$ to be equal to XB, PO must equal LO, obviously impossible unless $\phi=O$.

Conclusion. If, in operation, the pendulum moves in one plane then a line, the axis of which is the axis of rotation, O, of the pendulum, and not a plane will be projected correctly. If, however, the apparatus moves in a circular or spiral fashion about O then a point, the point O, and not a plane will be projected correctly. Using this method, then, it is impossible to project a true image of a plane.

Planigraphy (Fig. 2).

Description. The roentgen tube and cassette are mounted by the system AOB in such a manner that the focal spot of the tube and the plane of the film move in horizontal and parallel planes and describe linear, circular, or spiral movements or combinations of such movements. It is further required that the central ray lie on the line AOB.

Analysis:

From Figure 2

$$\tan\alpha=\frac{BA}{XB}$$

or

$$(A)\qquad XB=\frac{BA}{\tan\alpha}=BA\cot\alpha.$$

Now

$$\frac{X'B'+AA'}{LO+AA'}=\frac{BA}{OA}$$

or

$$(1)\quad X'B+AA'=\frac{BA(LO+AA')}{OA}$$

and

$$\frac{B'B+AA'}{AA'}=\frac{BA}{OA}$$

or

$$(2)\quad B'B+AA'=\frac{AA'\times BA}{OA}.$$

Now

(B) $X'B'=(X'B+AA')-(B'B+AA')$.

Substituting the values of (1) and (2) in(B)

$$X'B'=\frac{BA(LO+AA')}{OA}-\frac{AA'\times BA}{OA}$$

$$=\frac{BA}{OA}(LO).$$

Since

$$LO=OA\cot\alpha$$

$$X'B'=\frac{BA}{OA}\times OA\cot\alpha$$

(c) $$=BA\cot\alpha.$$

Therefore (c) is identical with (A).

That $B'Y'=X'B'=XB=BY$ also can be proved in a similar fashion.

The distortion of points above or below the plane LOM is shown diagrammatically. For example, points in the planes $L'M'$ and $L''M''$ are projected upon the film within the cone XAY and therefore are superimposed upon one another. However, from the position A'' it is seen that these points do not fall within the cone $X'A''Y'$ in all instances. All the points above and below the plane LOM are shifted a distance proportional to their distances above or below the plane, the angle ϕ, and the distances AO and OB. For example, the projection of M' is at Y'' which is outside of the line indicating the cassette, yet the projection of L' is at X'', well within the cassette. In the position A' the projection of L' will be outside of the cassette and M' will be well within, just the opposite from A''.

Conclusion. The planigraphic method is an excellent theoretical solution of the problem because the blurring of planes outside of the desired plane is possible in all directions due to the fact that a spiral or circular motion can be imparted to the system. The method has a number of serious difficulties, however, in practical application. The necessity of pivoting the roentgen tube in some sort of cradle and synchronizing its movements in such a manner that the central ray follows the line BOA in all positions of the system requires a complicated mechanism. Figure 2 illustrates this difficulty. In position A'', should the tube not be synchronized, then the beam at some points must come from the back of the target. Another difficult problem is the apparatus necessary to keep the roentgen tube and the film in perfectly parallel planes and always equidistant from each other. This type of apparatus must, of course, be much more elaborate than the one just described and the one which follows.

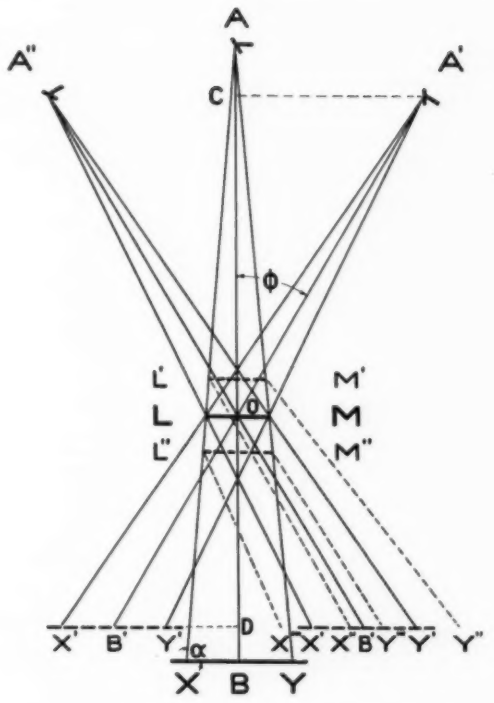

Fig. 3. Tomography (for explanation of figure see text).

Tomography (Fig. 3).

Description. The roentgen tube is fixed to the pendulum so that it is perpendicular to it at all times. The cassette, however, is suspended to the pendulum in such a manner that regardless of the angle, ϕ, the cassette is always parallel to the plane LM.

Analysis:

Assume for simplicity that

$$LO=OM$$

then

$$XB = BY.$$

Now

$$\tan \alpha = \frac{BA}{XB}$$

or

$$(A) \qquad XB = \frac{BA}{\tan \alpha} = BA \cot \alpha.$$

Now

$$\frac{X'D+CA'}{LO+CA'} = \frac{DO+OC}{OC}$$

or

$$(1) \qquad X'D+CA' = \frac{(LO+CA')(DO+OC)}{OC};$$

also

$$\frac{B'D+CA'}{CA'} = \frac{DO+OC}{OC}$$

or

$$(2) \qquad B'D+CA' = \frac{CA'(DO+OC)}{OC}.$$

Now

$$(3) \quad X'B' = (X'D+CA') - (B'D+CA').$$

By substitution of (1) and (2) in (3)

$$X'B' = \frac{(LO+CA')(DO+OC)}{OC} - \frac{CA'(DO+OC)}{OC}$$

$$= \frac{(DO+OC)}{OC}[(LO+CA') - CA']$$

$$= \frac{DO+OC}{OC}(LO)$$

$$(4) \qquad = \left[\frac{DO}{OC}+1\right]LO.$$

Now

$$(5) \quad DO = BO \cos \phi$$

and

$$(6) \quad OC = OA \cos \phi$$

and

$$(7) \quad LO = OA \cot \phi.$$

Substituting (5), (6), and (7) in (4)

$$X'B' = \left[\frac{BO \cos \phi}{OA \cos \phi}+1\right][OA \cot \alpha]$$

$$= \frac{BO}{OA} \times OA \cot \alpha + OA \cot \alpha$$

$$= (BO+OA) \cot \alpha.$$

But

$$BO+OA = BA.$$

Therefore

$$(B) \quad X'B' = BA \cot \alpha$$

which is identical with (A).

Similarly

$$\frac{Y'D+CA'}{DO+OC} = \frac{CA'-OM}{OC}$$

or

$$(8) \qquad Y'D+CA' = \frac{(DO+OC)(CA'-OM)}{OC}$$

$$(2) \qquad B'D+CA' = \frac{CA'(DO+OC)}{OC}$$

and

$$B'Y' = (B'D+CA') - (Y'D+CA')$$

or

$$B'Y' = \frac{CA'(DO+OC)}{OC} - \frac{(DO+OC)(CA'-OM)}{OC}$$

$$= \frac{DO+OC}{OC}[CA' - (CA'-OM)]$$

$$= \frac{DO+OC}{OC}(OM)$$

$$= BA \cot \alpha$$

which is identical with (A) and (B).

Conclusion. The analysis of this method proves that only points in a horizontal plane through O are projected without distortion while points outside of this plane

are projected with distortion, the distortion being proportional to the distances of the points above or below the plane through O, the angle ϕ, and the distances AO and OB. This method, while theoretically not as good as the planigraphic method because the movement of the system is linear and not circular or spiral and therefore distortion of disturbing planes is possible in only one direction, is the more practical of the two methods. The mechanical problem, compared to the planigraph, is very simple as the film cassette can be maintained in the horizontal position by a simple system of levers and no complicated mechanical system is necessary to maintain the central ray in the line AOB.

EXPERIMENTAL APPARATUS

The tomographic method, for the reasons cited above, was employed in the construction of an experimental apparatus. The fundamental design of the apparatus is quite similar to that which was described by Grossmann in his first communication on tomography. A schematic drawing of the apparatus is shown in Figure 4 while a photograph of the completed apparatus is shown in Figure 5.

The roentgen tube, A (Fig. 4), is firmly fixed to the pendulum B by means of the arm C. The cassette E is placed upon the tray D which is kept horizontal by means of the system of levers G. The tray D is pivoted at H. The cassette tray is so arranged that the plane of the film, shown as a dot and dash line in the cassette, is positively in the horizontal plane through the center of the pivot at H. This is necessary in order to prevent distortion due to change in position of the film.

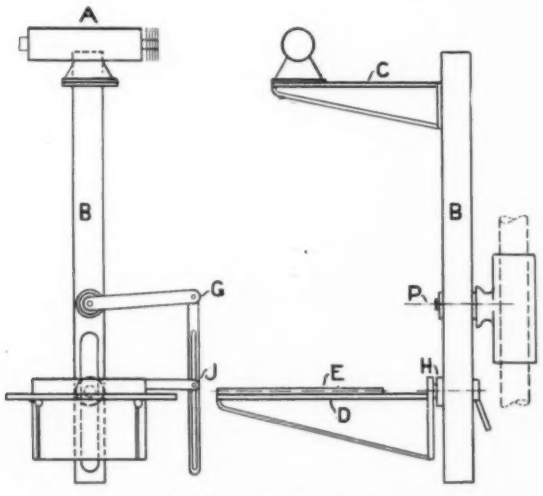

Fig. 4. Schematic drawing of the experimental tomograph.

Fig. 5. Photograph of the experimental tomograph.

The pendulum, or column B, is pivoted at P to a vertical standard as shown. A lead counterbalance is fixed to the lower end of the pendulum. In operation the pivot point, P, is adjusted to the desired plane of the object on the vertical standard. The cassette tray is then adjusted up or down in the slot in B, to give the minimum object to film distance, and locked at H. The cassette tray is then brought level by means of a spirit level and a lock at J. The apparatus is started by rotating the pendulum manually to the desired

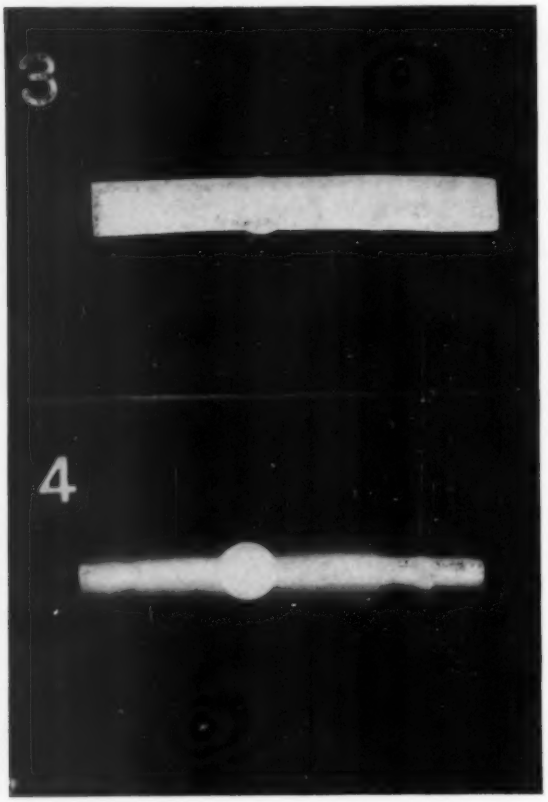

FIG. 6. Experiment No. 3. The image of the lead circle is obliterated by the image of the superimposed lead strip in ordinary roentgenography. Experiment No. 4. The image of the lead circle is distinct while the image of the superimposed lead strip is almost obliterated using the tomographic method of roentgenography.

angle, the counterweight causing the apparatus to oscillate when the pendulum is released.

EXPERIMENTAL PROOF

Many experiments were performed with sheets of lead 1 mm. thick and of various sizes and shapes to determine whether or not the apparatus as constructed would actually project a plane surface without distortion.

The "target-plane" distance of the experimental apparatus is fixed at 82 cm. while the "plane-film" distance is variable between 10 and 30 cm. The period of the apparatus is 3.3 seconds and the time of the exposure in these experiments was five seconds, the pendulum describing an initial arc of 60 degrees and being allowed to oscillate freely during the five second exposure. The exposure was timed by a standard mechanical timer. In the following series of experiments the plane-film distance was 14 cm. except in No. 8 where it was 9 cm.

The following series of experiments was performed:

(1) *Experiment.* A 4 cm. lead square was placed at the absolute center of the axis of rotation of the pendulum and the plane of the film was at the absolute center of the axis of rotation of the cassette holder. The exposure was made with the apparatus in motion under the conditions enumerated above.

Result. An image of the lead plate was projected on the film without distortion except that due to the divergence of the rays.

Conclusion. A true image of a plane surface can be projected on a film without distortion with the tomographic apparatus.

(2) *Experiment.* As in (1), above, except that the plane of the film was 4 mm. below the absolute center of the axis of rotation of the cassette holder.

Result. The image of the lead plate was projected on the film but the image was blurred along the edges which lay parallel to the axis of rotation of the pendulum.

Conclusion. This experiment demonstrates that the plane of the film must lie in the absolute center of the axis of rotation of the cassette holder or distortion of the projected plane will result.

(3) *Experiment.* A lead circle 1 cm. in diameter was placed at the absolute center of the axis of rotation of the pendulum and a lead strip of dimensions 85 × 10 × 1 mm. was placed 1 cm. directly above the circle, the long axis of the strip lying parallel to the axis of rotation of the pendulum. An exposure was made with the apparatus stationary.

Result. The image of the circle is obliterated by the image of the superimposed lead strip (Fig. 6).

(4) *Experiment.* As in (3), above. An exposure was made with the apparatus in motion under the conditions enumerated above.

Result. The image of the lead strip is almost completely obliterated by blurring while the image of the circle is distinct (Fig. 6).

Conclusion. The image of a preselected plane

may be projected without distortion while the images of superimposed parts which obscure or obliterate the image of the desired plane in the usual roentgenographic method can be partially or completely eradicated by the tomographic method.

(5) *Experiment.* The 4 cm. lead square was placed at the absolute center of the plane of the axis of rotation of the pendulum but the center of the lead square was 8 cm. distant from the line of the direct beam in the direction perpendicular to the axis of rotation. The exposure was made with the apparatus stationary.

Result. An image of the lead square was secured for comparative purposes.

(6) *Experiment.* As in (5), above. The exposure was made with the apparatus in motion under the conditions enumerated above.

Result. A slightly blurred image of the lead plate was projected on the film, the image being blurred along the edges which lay parallel to the axis of rotation of the pendulum.

Conclusion. The blurring was slight and was interpreted as being due to the fact that the square is not a plane but has a significant (1 mm.) thickness. This experiment demonstrates that a correct image of points on a plane some distance from the central ray can be projected without distortion.

(7) *Experiment.* As in (1), above, except that the margins of the square were diagnonal to the axis of rotation of the pendulum. An exposure was made with the apparatus in motion under the conditions enumerated above.

Result. An image of the lead square was projected on the film without distortion.

Conclusion. The direction of lines within a plane has no influence on the correctness of the projected image of the plane.

(8) *Experiment.* As in (7), above, except that the plane-film distance was changed from 14 cm. to 9 cm. An exposure was made with the apparatus in motion under the conditions enumerated above.

Result. An image of the lead plate was projected on the film without distortion except that due to the divergence of the rays.

Conclusion. This experiment demonstrates that the plane-film distance has no influence upon the correctness of the image except that which is due to the divergence of the rays.

SUMMARY

(1) Mathematical analyses of the three chief planigraphic methods are presented which show that the stratigraphic (Vallebona) method is faulty but that both the planigraphic (Ziedses des Plantes) and the tomographic (Grossmann) methods offer a correct solution of the problem presented in the roentgenographic projection of a true image of a plane section of a solid object.

(2) The planigraphic method offers a better theoretical solution of the problem than the tomographic method because interfering parts can be blurred in all directions by imparting a circular or spiral motion to the apparatus while with the tomographic method interfering parts can be blurred in only a linear direction.

(3) The mechanical problems in the construction of the planigraph are, however, greater than in the construction of the tomograph and the theoretical advantages of the former probably do not outweigh the mechanical advantages of the latter.

(4) The authors' experimental tomograph is described.

(5) Experimental proof is offered to show that the authors' tomograph will project a correct image of a predetermined plane section of a solid object while the images of superimposed parts which obscure or obliterate the image of the desired section in the usual roentgenographic method can be partially or completely eradicated.

THE RHOMBOID FOSSA OF THE CLAVICLE*

By EUGENE P. PENDERGRASS, M.D., *and* PHILIP J. HODES, M.D.
PHILADELPHIA, PENNSYLVANIA

THE clavicle is heir to many anomalies, some of which are of importance to the roentgenologist. The more common anomalies, cleidocranial dysostosis, and agenesis or hypoplasia of the clavicles have been repeatedly described in the literature. Unilateral[5] and bilateral[1] pseudarthrosis, while not as well known, have also received recognition. The anomalous "canalicule claviculaire,"[6,7] which pierces the clavicle carrying branches of the supraclavicular nerve, is of no importance to roentgenologists because its small lumen traverses the clavicle diagonally, making its visualization impossible. Piersol[4] and later Parsons[3] called attention to the difference in length which occurs normally between both clavicles. Both authors have attributed the greater length of the left clavicle to the increased curvature of the right resulting from the more extensive use of the right arm. The right clavicle usually has a greater density and thickness than the left.

Our interest in the "rhomboid depression" was stimulated by an unusual appearance in the clavicles of a healthy adult male (Fig. 1). The condition was considered an anomaly because the patient was without symptoms and there was no history of previous trouble in this region. Dr. O. V. Batson, Professor of Anatomy in the Graduate School of Medicine of the University of Pennsylvania, was consulted and it was his belief that the clavicular defect was due to the impression of the rhomboid ligament which in our cases was unusually well developed (Figs. 2–7).

The "rhomboid depression," also called "rhomboid impression" and tuberalis costalis, is situated on the inferior surface of the clavicle. It is a "broad, rough surface, rather more than an inch in length, for the attachment of the costoclavicular (rhomboid) ligament"[2] (Fig. 2). According to Parsons,[3] 10 per cent of the clavicles he studied had a rough irregular depression for attachment of the rhomboid ligament, and in some instances the depression may be 1 cm. deep and may penetrate half way through the thickness of the bone.

Frequently the rhomboid impression (Figs. 2–4) may not be seen on the roentgenogram but occasionally a fossa or irregular defect can be recognized easily (Figs. 5–7). It lies along the inferior surface about 1 to 1.5 cm. from the sternoclavicular junction and usually measures about 2 to 2.5 cm. across its greatest width. In one instance the cleft was much wider (Fig. 9), measuring almost 4 cm. across its greatest width. Sometimes the depression appears to lie more anteriorly or posteriorly, enabling one to see normal clavicle below the bone defect (Fig. 8). As a rule, the superior border of the defect is formed by a narrow irregular zone of increased density (Fig. 10). The upper border is usually irregular and has a ragged, sawtooth appearance. In some instances it may be more smoothly molded (Fig. 11). The depression is frequently bilateral (Fig. 1), though one side may stand out more clearly than the other, but it may occur on one side, as seen in Figure 8.

The rhomboid depression resembles a destructive bone lesion and should therefore be of interest to the roentgenologist. It may be necessary to differentiate it from a metastatic focus of infection in patients with chronic osteomyelitis or with blood stream infections (Figs. 12 and 13), tuberculosis, syphilis, metastatic carcinoma, sarcoma or Ewing's tumor. The lack of symptoms and the usual bilateral occurrence of the anomaly are of importance in distinguishing it from other conditions.

* From the Department of Radiology, Hospital of the University of Pennsylvania, Philadelphia.

The rhomboid depression reported in this series has occurred only in muscular males but there seems to be no good reason why it should not occur in females. No studies have been made to determine whether it is hereditary. It has been detected accidentally in the chest films and it is entirely possible that the anomaly may occur not infrequently.

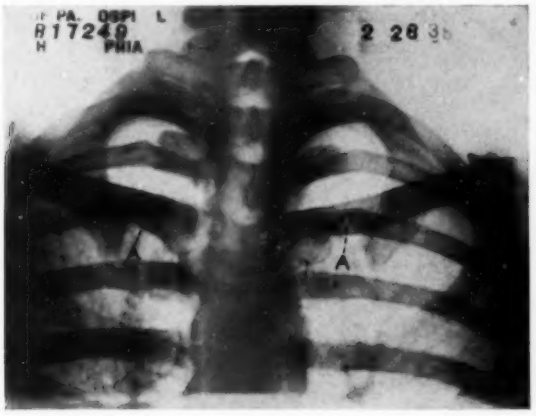

Fig. 1. Case 1. Example of bilateral rhomboid depressions. These are seen at *A*.

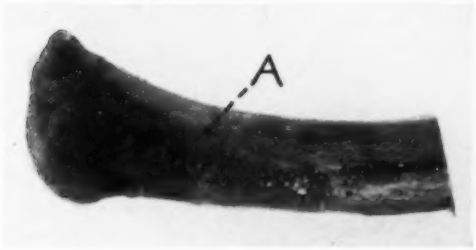

Fig. 2. Sternal end of the clavicle seen from below. *A* demonstrates the attachment for the rhomboid ligament with the formation of the rhomboid impression. (Specimen loaned by Dr. O. V. Batson.)

Fig. 3. Roentgenogram of the same specimen seen in Figure 2.

Fig. 4. Roentgenogram of the specimen seen in Figure 2. Examinations made in different positions showed nothing suggesting a rhomboid depression.

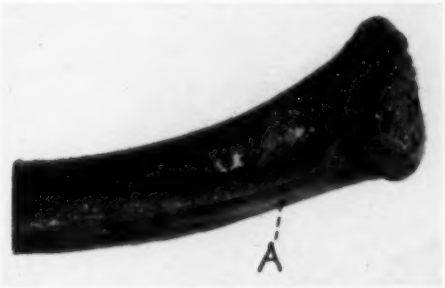

Fig. 5. Sternal end of the clavicle with a rhomboid depression. *A* demonstrates the attachment for the rhomboid ligament with the formation of the rhomboid depression (fossa). (Specimen loaned by Dr. O. V. Batson.)

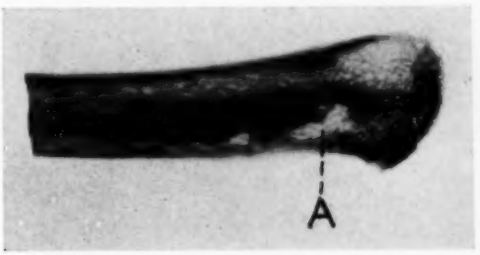

Fig. 6. Roentgenogram of specimen illustrated in Figure 5.

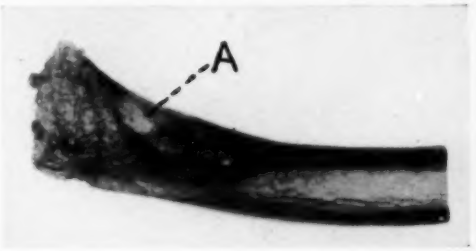

Fig. 7. Roentgenogram of the specimen seen in Figure 5. Examinations made in different positions demonstrating the rhomboid depressions at *A*.

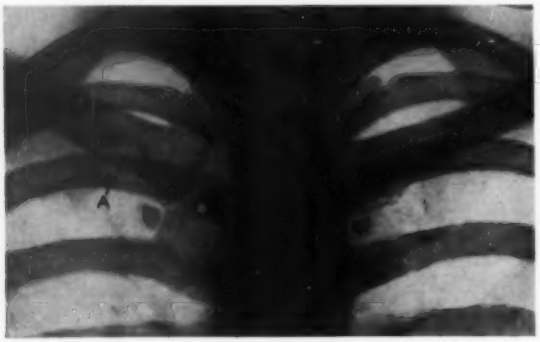

FIG. 8. Case II. Unilateral rhomboid depression seen at *A*.

FIG. 9. Case III. This is the largest rhomboid depression we have seen. Note the many prominent fossae within the rhomboid depression at *A*.

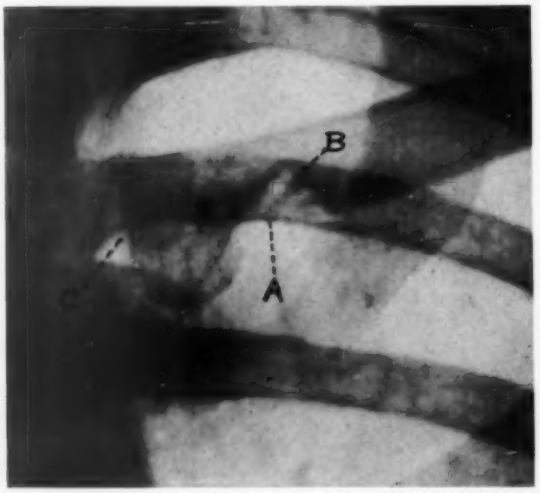

FIG. 10. Close-up of the left clavicle seen in Case I. Note the cleft-like appearance at *A*. Note the bone eburnation at *B*, with the ragged, saw-tooth appearance. *C* demonstrates the sternoclavicular articulation.

FIG. 11. Case IV. Note the rhomboid depression at *A* and the bone eburnation at *B*. Note the more smoothly molded appearance of the apex of the defect.

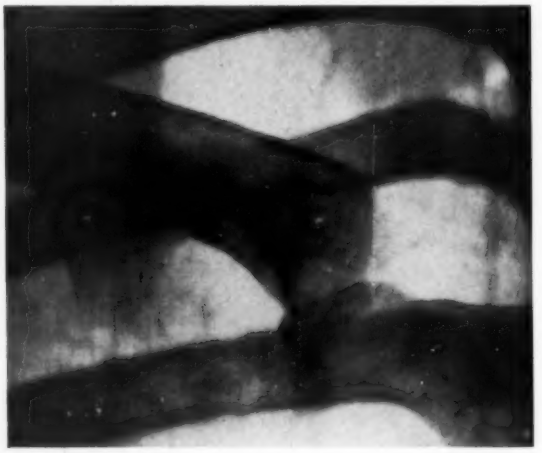

FIG. 12. Close-up of the right clavicle seen in Case I. Note the more smoothly molded contour in comparison with the left clavicle demonstrated in Figure 10.

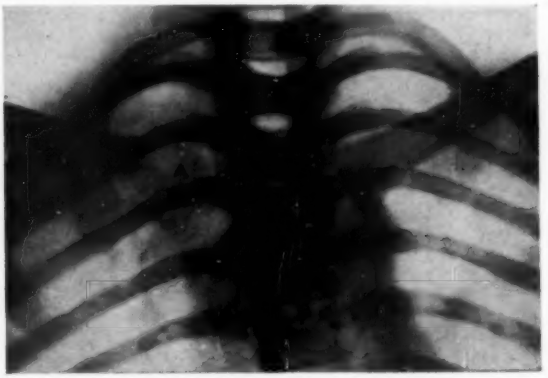

FIG. 13. Bone destruction at *A* due to osteomyelitis.

SUMMARY

1. The rhomboid depression, an anomaly of the clavicle, is described.

2. This anomaly may simulate a bone destructive lesion.

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INCREASING THE VALUE OF INTRAVENOUS UROGRAPHY BY IMPROVEMENTS IN TECHNIQUE

By R. A. BERGER, M.D.
RICHMOND, VIRGINIA

TECHNICAL difficulties probably account for the greater portion of failures in intravenous urography rather than the inadequately and poorly functioning kidney. It is true that there are certain limitations which will be encountered, but some of these may be circumvented by more care in the beginning of the examination and a little more thought in the preparation of the patient.

Exercising three simple principles should produce a diagnostic excretory study of the urinary tract in all cases in which there is some semblance of a kidney function. These principles are: (1) proper preparation of the patient; (2) injection of an adequate amount of diodrast; (3) accurately located and maintained abdominal pressure. We have routinely employed the following procedure in preparing a patient for an intravenous urographic examination.

The individual receives no fluids by mouth from midnight prior to the examination on the following morning. Prohibiting fluids has enhanced materially the success of this examination since it allows for greater concentration of the iodides by minimizing as far as possible diluents in the excretory system. It is not believed that abstinence from fluids for this period produces an undesirable effect on the excretory function of the kidney and conversely it is not supposed that preliminary forcing of fluids is of aid in the production of better pyelograms. Some feel that forcing fluids stimulates the kidneys to greater activity and thereby causes a more rapid excretion of the diodrast. But by increasing the liquid intake, the concentration of the contrast substance is lost to some degree and we believe that this loss is not desirable. Therefore we restrict the fluid intake. We do permit the patient to have a small glass of orange juice in the morning. This supplies enough liquid and nourishment to carry the patient through the examination with the least amount of discomfort from thirst and hunger. No other foods are given. The orange juice is sufficient to care for the patient's immediate needs and it offers enough stimulation to the gastrointestinal tract to force along retained material and gases.

The patient's gastrointestinal tract must be cleared of all possible gas and retained materials. This is accomplished by catharsis and enemas. Laxatives of a mild nature are preferable and particularly those which do not produce a great deal of gas. Plain and bland enemas are more desirable. By cleansing the enteric system one great difficulty in the production of a diagnostic film is overcome. Aside from producing better roentgenograms, this method makes the patient more comfortable, since tight abdominal pressure, which is necessary, does not produce abdominal pain and discomfort when the patient is on the examining table.

When the patient is properly placed for roentgenography and the preliminary film has been studied for possible leads and for the presence of objectionable material in the zones in question, the dose is decided. We have routinely used 30 c.c. of diodrast in the study of adults. In more than 150 cases examined in the last year there have been no mishaps, untoward symptoms or reactions. More than 70 per cent of these examinations were performed in the office and the patient was allowed to leave immediately after the last film had been viewed and the examination considered concluded. For children, a dose of 20 c.c. of diodrast has been used, with similar re-

sults. The larger amount of contrast substance has been of material aid in the production of a valuable diagnostic film. By giving the larger amount of intravenous material and inhibiting fluids in the beginning of the examination, there certainly appears to be a greater density of the pyelographic shadow.

The production of a good pyelogram is dependent on the concentration of the substance and the amount of the contrast material present. To have sufficient diodrast in the excretory pathways, pressure, and properly applied pressure, is the prime essential. The various pressure devices described in the literature have been utilized but have been found unsuitable for one reason or another. One made of a very light non-opaque wood produces unnecessary pain at the sites of the wooden promontories; those of rubber balls produce unnecessary shadows. The air-filled balloon alone is not sufficient. In addition to the latter, an ordinary bed sheet rolled into a tight bundle, just large enough to fit between the iliac crests, has proved very satisfactory. It is imperative that the sheet does not encroach on the bony prominences of the pelvis. If this occurs tight pressure cannot be maintained for a period long enough to obtain satisfactory results. If the sheet is properly folded and placed, the patient will tolerate a continued pressure for a considerable period. When the sheet is placed immediately above the symphysis pubis and so situated that it lies directly over the sacrum and the prominence of the pelvis posteriorly, a uniform and sufficient pressure can be maintained, which is fairly comfortable for the patient. The air-filled balloon is placed above the sheet and beneath the restraining band on the Potter-Bucky diaphragm. Tightening the band as much as the patient can comfortably tolerate will permit complete occlusion of the ureters in thin and well-nourished individuals and very satisfactory blocking is secured in stout patients. If the sheet is of a good grade and not starched the shadow cast by it is negligible.

It is possible by this means to obtain a complete filling of the urinary tract above the bony pelvis with little or no contrast substance below the point of maximum ureteral compression. At times, it has been found that the left excretory pathway is not so well occluded as the right side. The explanation for this seems to be on an anatomical basis. The ureter on the left side lies beneath the sigmoid flexure and its heavy mesenteric root. In well-nourished individuals this is undoubtedly firm enough to prevent a ureteral compression by outside pressure. This may also account for the less frequent occurrence of left-sided pyelectasis in pregnancy.

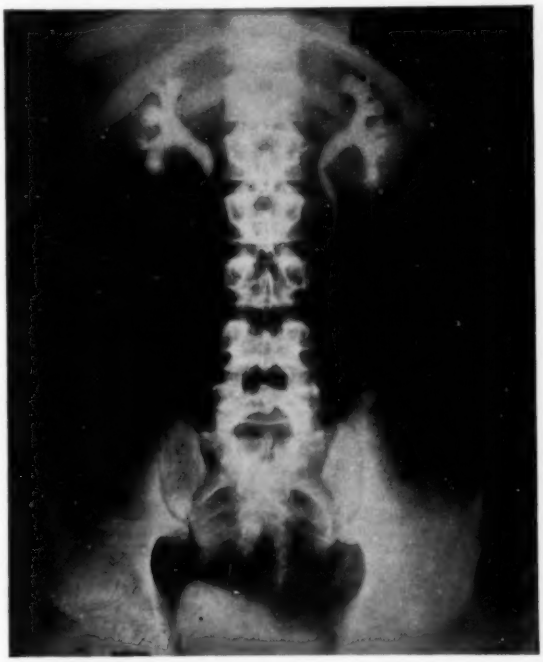


Fig. 1. Normal intravenous pyelographic study.

Having observed the foregoing steps and applied the tight pressure immediately after the injection of the diodrast, one should obtain excellent bilateral studies as far as the kidney function will permit. The normal filling should reveal ureters down to the point of pressure, well filled and sharply outlined pelves and calyces. The kidneys will be more apparent due to the presence of the diodrast in the blood-filled

FIG. 2. Demonstration of a poorly prepared patient.

FIG. 3. Same patient as in Figure 2 properly prepared.

organs. Releasing the pressure and allowing a few minutes for the upper urinary tract to empty into the lower, one can obtain a good visualization of the lower ureters and bladder.

FIG. 4. A retrograde pyelographic study. There is inadequate filling. The diagnosis is obscure.

FIG. 5. Same patient as in Figure 4. Note the joined pelves and the ureter extending down from the lower pelvis.

Fig. 6. A well-shown anomaly.

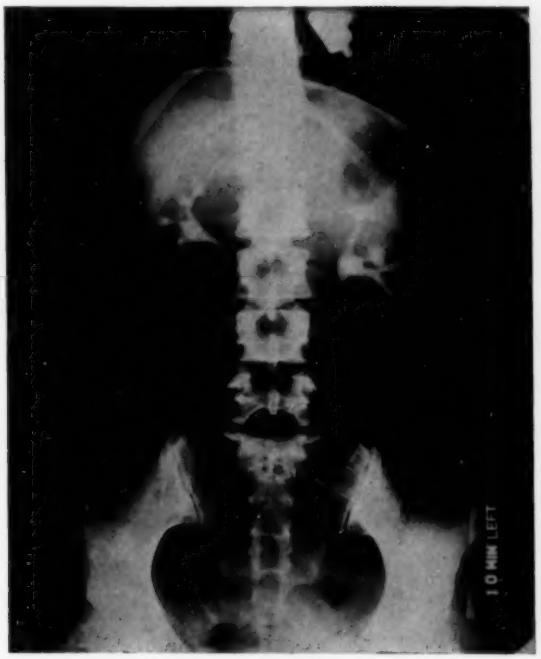


Fig. 7. Minor changes in the left mid-calyx well shown by the intravenous method.

Figure 1 represents a normal pyelographic study in a large muscular man. In the absence of gas due to preliminary preparation, an excellent pyelogram is obtained. The concentration of the iodide is excellently shown, no doubt aided by prohibiting fluids. The pressure has retained enough of the contrast substance in the

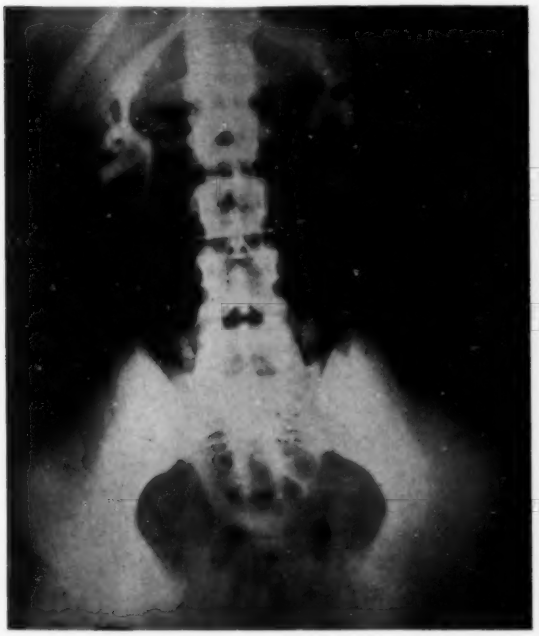


Fig. 8. Early changes due to tuberculosis in the left mid-calyx area.

Fig. 9. Advanced changes due to tuberculosis.

calyces and pelves to fill them perfectly. There is no overdistention and we have never been troubled by the conflicting pyelovenous backflow sometimes encountered in the retrograde method.

In Figure 2 a faint kidney shadow is visualized on the left side with all detail within the abdomen obscured by gas. This case represents an attempt to examine a patient who has had no preparation whatever. Only two of the three principles were followed: pressure and dosage. But the three must be combined to obtain a successful study. Figure 3 shows the same ten year old boy two days later after adequate preparation. In this study the three conditions were fulfilled, and the end-result is satisfactory. Disregarding one of the three principles has resulted in failure in our experience.

At times the intravenous method is of inestimable value in defining cases which are incompletely visualized by the retrograde method. Figure 4 demonstrates a direct filling of the left kidney. The urologist was limited in his efforts because of pain which the patient suffered, a definite indication for the cessation of further pelvic distention. The film revealed evidence of an anatomical variant, but the true nature of the anomaly was not apparent. Following this examination by a well-controlled intravenous study the exact picture of the condition was revealed, as shown in Figure 5. The true pelvis is connected by a broad isthmus to a secondary pelvis from which the ureter extends downward.

Other anomalies (Fig. 6), as far as the kidney function will permit, can be accurately determined by the intravenous method with the least possible chance of overlooking some aberrant process. This is an important contribution to urological examinations inasmuch as anomalous processes are subject to pathological changes.

Minor pathological changes can be and are being shown by the excretory method with much success, principally because of improved technique. Figure 7 demonstrates a minor change in the isthmus of the mid-calyx. By the retrograde method this might be attributable to inadequate filling or to injected air. The former is not likely with a well-controlled procedure, and the latter not possible by the intravenous method. The exclusion of introduced air does away with a troublesome and conflicting shadow.

Recently an excretory study disclosed the very early changes of renal tuberculosis which were not apparent on a satisfactory pyelogram. We feel certain that this method of procedure was the determining factor in bringing out the pathological changes, the etiology of which was determined by demonstrating the tubercle bacillus in the urine. Figure 8 reveals early tuberculous changes in the mid-renal area, while Figure 9 demonstrates more advanced changes.

Hydronephrosis, cysts, tumors, renal carbuncles, calculi and other disease entities lend themselves to excretory study with considerable diagnostic accuracy, particularly in the determination of stones as to their location and the extent of the renal damage. By serial and angle films the examiner is able to give to the urologist accurate information regarding the position of the calculus and its effect upon the kidney substance and function. This is not as easily obtained in the other method since there is not a continuous supply of contrast substance in the excretory pathways.

There is no fixed time interval between exposures. After the intravenous injection has been made and the pressure appliance is fitted and tightened to the proper degree, the first exposure is made. This is roughly a five minute film. It is processed and as soon as it can safely be viewed under lights it is examined. Sufficient information can often be obtained from this film to determine the subsequent course. In case of normal kidneys enough data are obtained from this single examination to warrant an early conclusion. If the first roentgenogram indicates a badly functioning kidney, longer intervals are required between ex-

posures. In the meantime, the abdominal pressure is maintained. Where stones are present, every effort is made to locate them and to determine secondary kidney manifestations. Mass lesions in the kidneys often impede the excretory ability, which makes it necessary to increase the time of the exposure interval. In some kidneys which display poor function on the first films we have been able to demonstrate very good filling in the excretory pathways as much as four hours later. This has taught us to entirely disregard a definite film interval such as the fifteen, thirty and forty-five minute film method. The intravenous examination requires the absolute personal supervision of the roentgenologist. Every film made is observed before the subsequent film is taken. This is of such extreme importance that it cannot be neglected, just as a roentgenoscopic examination cannot be neglected in a gastrointestinal study. By this personal contact and supervision of each case, there is no question that the value of this method is greatly enhanced.

During the entire examination some individual is required to remain near the patient to watch for abnormal reactions if such should occur. Elderly patients and those with elevated blood pressures do not tolerate abdominal pressure as well as other patients. Marked hypertension is an indication for caution in the application of tight and prolonged pressure.

I have watched this technique with considerable interest since my association with Dr. Fred M. Hodges. It is without doubt superior to the procedures commonly accepted and employed in many clinics.

CONCLUSIONS

1. The value of an intravenous urographic study is materially increased by employing three simple and adaptable principles.

2. The employment of these principles permits better visualization of the excretory pathways by the elimination of gas, by greater concentration of the contrast substance in the excretory system, and by better filling due to adequate ureteral compression.

3. In our experience it is just as frequently necessary to check a retrograde by the intravenous method as it is to check an intravenous examination by the retrograde method.

THE TREATMENT OF HYPOPHYSEAL STALK TUMORS BY EVACUATION AND IRRADIATION*

By RALPH C. CARPENTER, M.D., GEORGE W. CHAMBERLIN, M.D., *and* CHARLES H. FRAZIER, M.D., Sc.D.
PHILADELPHIA, PENNSYLVANIA

INTRODUCTION

BEFORE entering upon the subject matter of this communication, namely, the *treatment of hypophyseal stalk tumors*, let us define precisely what we mean by the term "hypophyseal stalk tumor." Those familiar with the literature of parasellar tumors realize that there is an unquestionable disagreement as to the classification and nomenclature of these tumors. Until a short time ago these tumors were rather loosely grouped into two separate divisions: the Rathke pouch tumor and the craniopharyngeal duct tumor (see Fig. 1) or the so-called craniopharyngioma. The distinction between these was rather vague, and in many cases it appears that no effort was made to distinguish between the two types and the two terms were used interchangeably.

That there were reasonable grounds for making a distinction in the nomenclature of the various types of tumor would seem evident from the editorial comment[3] which appears in the *Journal of Neurology and Psychopathology*, January, 1936, in which the following statement is made:

To the name "craniopharyngioma" there have been strong and well-grounded objections, and it is surprising that it still has a certain vogue. Frazier and Alpers have recently attacked this term, and have suggested that the suprapituitary epitheliomas should be called "tumours of the hypophyseal stalk," and should be clearly distinguished from the simple cysts in this region, for which they suggest the term "tumours of Rathke's cleft." Whether it is always possible to make so sharp a distinction seems doubtful, as a small area of epitheliomatous tissue is often present in what are otherwise simple cysts, but the general principle of the suggested nomenclature is sound. Although the name "tumour of the hypophyseal stalk" carries no suggestion as to the histological structure of the tumour, i.e. whether epitheliomatous or gliomatous, in view of the fact that many such tumours contain both types of tissue this may not be a disadvantage.

These questions of nomenclature have more than an academic interest, since clarity of thought is bound up with language. It is probable that the classification of the future will lay greater emphasis on the malignancy and rate of growth of the tumours, and that it will indicate more clearly which tumours arise from congenital "cell-rests" and which from normal adult cells.

In 1934, one of us (Frazier[4,5]) proposed a new classification based on anatomical, embryological and histopathological differences. The term "hypophyseal stalk tumor" was advocated instead of craniopharyngioma on the grounds that craniopharyngioma was a misnomer. This tumor has no relation to the pharynx and takes its origin from an anlage (see Fig. 2) of the original stalk from the buccal cavity. It becomes cystic and the wall of the cyst is characterized histologically by a lining membrane of modified squamous epithelial cells (Fig. 3). As for the term, Rathke pouch tumor, the term "Rathke cleft tumor" was proposed, based on the well-known fact that the original Rathke's pouch becomes converted into a solid structure, in reality the pars anterior of the hypophysis; a small cleft remains between the pars anterior and the pars posterior, and it is from this cleft that this tumor has its origin.

PATHOLOGICAL DISCUSSION

These stalk tumors may be divided into two groups, according to whether they

* From the Neurosurgical Clinic and the Department of Roentgenology, University Hospital, Philadelphia.

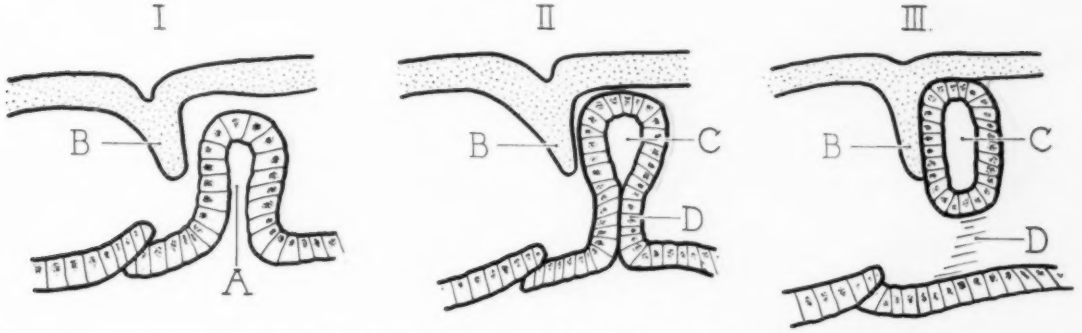


Fig. 1. Diagrammatic sketch of the development of the hypophysis from the buccal cavity. *I.* The original invagination from the buccal cavity, *A*. *II.* Communication with the buccal cavity, obliterated at *D*, the structure from which the anterior lobe arises at *C*. *III.* The remnant of stalk, *D*, the anterior lobe, *C*, in close relation with the infundibular process, *B*.

take their origin from the upper or from the lower anlage. These two groups of tumors differ in many respects: in their clinical aspect, in their relation to the optic chiasm and in their relation to the third ventricle.

Those which take their origin from the higher cells are difficult, if not impossible, of access on the operating table; they soon block the third ventricle and cause all the signs of increased intracranial pressure and usually cause a secondary or post-papillitic atrophy.

The following is an example of a case of the hypophyseal stalk tumor under consideration:

Case 1. *Summary.* A child, aged twelve, with a left hemiparesis and left hemianopia, with signs of pituitary dysfunction; dwarfism, adiposity, amenorrhea were the most conspicuous. A suprasellar cyst was evacuated through the first temporal convolution with disappearance of the hemiparesis and improvement of vision from 6/12 to 6/9. Recurrence of hemiparesis, May, 1934. Cyst evacuated for the second time and a course of roentgen treatment instituted. Since May, 1934, there has been no sign of recurrence, a period of twenty-five months, and the patient is now practically symptom-free except for the dwarfism and amenorrhea.

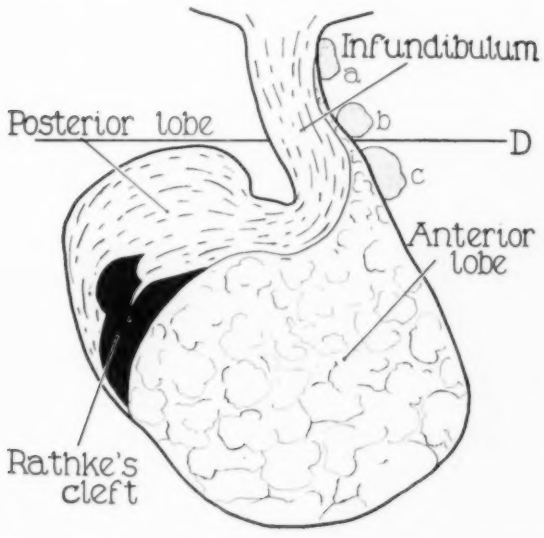


Fig. 2. Anatomical drawing to show the various constituents of the fully developed hypophysis. Note the location of Rathke's cleft between the anterior lobe and the posterior lobe.

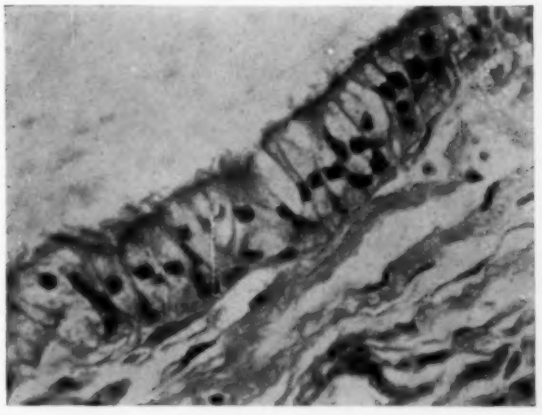


Fig. 3. A high power photomicrograph showing the ciliated cells with their vacuolated cytoplasm and their stout cilia. Hematoxylin and eosin stain.

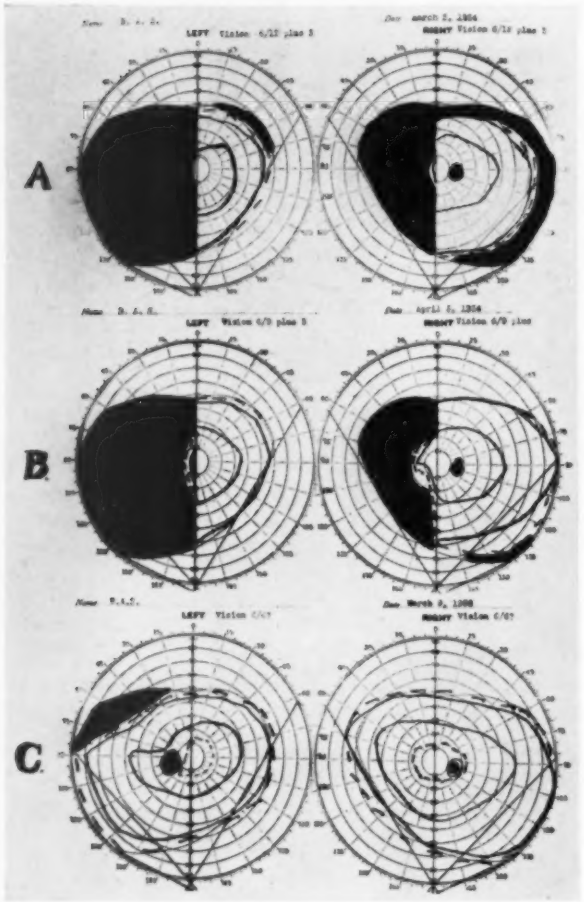


FIG. 4. Case 1. *A*. March 3, 1934. Before first operation: vision, O. S. 6/12 plus 3; O. D. 6/12 plus 3. Fields: complete left homonymous hemianopsia. *B*. April 5, 1934. After first operation: vision, O. S. 6/9 plus 3; O. D. 6/9 plus. Fields: extensive left homonymous defect (slight improvement). *C*. March 9, 1936, two years after treatment begun: vision, O. S. 6/6 (?); O. D. 6/6 (?). Fields: left homonymous hemianopsia has disappeared. Fields almost full.

B. A. S., female, aged twelve (File No. 28582), was referred to the Neurosurgical Service by Dr. A. M. Ornsteen and Dr. Frederick Tilney March 2, 1934, complaining chiefly of dwarfism and a left hemiparesis.

History Present Illness. Without any history of endocrine dysfunction in the family, with a father, mother and two brothers, living and well, at the age of five the child fell down stairs and remained unconscious for twenty-four hours. When six years old (1928) she developed persistent nausea, vomiting, polyuria, and polydipsia. These continued for two years. The mere sight of food nauseated her; she drank large quantities of fluids and passed as much as 8 pints of urine a day. At this time she was undersized, had a thick torso, coarse skin and brittle hair; no axillary or pubic hair.

Possibly as the result of glandular feeding two years later (1930), she seemed to improve; there was a slight increase in stature, nausea ceased, the polyuria diminished and her appetite became voracious. However, with this improvement she began to have severe headaches, at first intermittent, gradually increasing in frequency until now they occur daily and may last eight hours. From this time until the present (1930–1934) her mental faculties have been undisturbed. In fact, she might be said to be precocious, and in her studies, her games and music she was more than abreast of her classmates.

From December, 1933, to February, 1934, she developed gradually a left hemiparesis and a left temporal hemianopia. The left pupil became larger than the right and there was an occasional fleeting tinnitus in the left ear.

Neurological Examination. Spastic left hemiparesis, increase in left patellar and Achilles tendon reflexes and a positive left Babinski; dysdiadokokinesia, left; left pupil larger than right.

Endocrine Studies. Dwarfism, the child at the age of twelve has the stature of a six year old; adiposity chiefly of torso; absence of axillary and pubic hair but a fine lunago-like fuzz covering the back and posterior portions of arms and legs; amenorrhea, the child has never menstruated; tendency to somnolence; basal metabolism minus 12.

Ophthalmic Examination. A left homonymous hemianopia; vision O. S. and O. D. 6/12; no papilledema (see Fig. 4).

Roentgen Examination. A suprasellar midline calcified area 2×2.5 cm. with erosion of posterior clinoid processes.

Preoperative Diagnosis. Hypophyseal stalk tumor.

Operation, March 10, 1934. Right temporofrontal craniotomy, avertin anesthesia (Frazier).

As the dura was exposed, we observed that the brain was not very tense, much less in fact than we had anticipated finding it. However, in order to facilitate exploration, the patient was given 50 c.c. of 50 per cent glucose intravenously. To facilitate our exploration the bone was removed from beneath the temporal

muscle; at places it was not thicker than heavy paper, probably because of the long-continued pressure.

After the wound covers were applied, we proceeded with the exploration and inspected first the region of the optic nerves and chiasm and the sella turcica. Nothing abnormal was seen. The chiasm did not appear to be pushed forward, but occupied its normal position. Thinking the patient might have a suprasellar cyst which could be reached only through the frontal lobe, a cannula was passed through the frontal lobe in the direction of the sella, with negative results.

It was then decided to approach the suprasellar region. A small cannula was passed directly inwards through the first temporal convolution 1 cm. below the Sylvian vessels, and 4 cm. from the surface the cannula penetrated the wall of a cyst from which was evacuated over 30 c.c. of a dark reddish fluid filled with what were believed to be cholesterin crystals. The site of the puncture was marked on the cortex by four silver clips, arranged in the shape of a cross, to serve as a guide to the site of puncture should another evacuation be necessary. With this we decided to proceed no further. The patient seemed to stand the operation very well. The blood pressure did not vary more than 10 points and, although she had a little ether while we were closing the wound, she recovered consciousness before she left the operating room.

Operative Diagnosis. Hypophyseal stalk tumor.

When the patient was discharged from the hospital April 19, 1934, the hemiparesis and headache had entirely disappeared, the hemianopia partially so and the vision had improved from 6/12 to 6/9 in each eye (see Fig. 4).

Second Admission, May 29, 1934. Two weeks ago the hemiparesis recurred. In other respects her condition was about the same except that there was a much smaller field cut.

Operation, June 11, 1934. Evacuation of cyst (Frazier). Through a short vertical incision, using the silver clips applied at the first operation as a guide, the cannula was introduced, penetrated the cyst wall and 60 c.c. of a thick yellowish fluid with cholesterin crystals withdrawn. Before closing the wound air was injected into the cyst cavity and a roentgenogram taken to further identify the exact location and size of the cavity (see Fig. 5).

Fig. 5. Case 1. Roentgenogram made immediately following second operation, showing cyst filled with air (see operation notes).

Immediately after the operation the facial asymmetry had largely disappeared and on the following morning the grip of the left hand was much stronger.

Discharged, June 16, 1934.

Before the patient's discharge from the hospital on April 19, 1934, we discussed with Dr. H. K. Pancoast the propriety of irradiation to prevent refilling of the cyst. In response to this inquiry, Dr. Pancoast wrote:

> I have received your communication in regard to the possible treatment of the pharyngeal pouch cyst case. I do not know what the effect would be on this case. Presumably the cyst is lined with epithelium and there might be some effect upon the secretion. So far as I could see, there would be no harm in trying the treatment, any more than there would be in treating any ordinary case of a similar nature, especially the pituitary cases. The only bad effect would be from the removal of the hair, which would be bound to occur.

Accordingly, with Dr. Pancoast's approval, the roentgen treatment was begun and between May 21, 1934, and July 7, 1934, the patient received 1,600 r to each one of three portals over the head. Tumor dose: 2,844 r; period of treatment forty-seven days.

September 5, 1934. Hemiparesis almost disappeared; patient now able to continue her studies on the piano.

The patient had been disturbed a good deal

FIG. 6. Case I. Photograph of patient, March 18, 1936, two years after treatment was begun: facial symmetry restored.

during the day, and her sleep particularly at night, by the polyuria. With the aid of a posterior lobe powder insufflated in the posterior nares with a special deVilbis atomizer, the polyuria was in large measure controlled.

In the fall of 1934, under the care of Dr. Irving H. Pardee of New York, she was given an intensive course of glandular therapy, which included anterior and posterior lobe pills, three of each a day and a hypodermic injection of 1 c.c. of phyone three to five times a week. By January 30, 1935, the patient had increased ¾ inch in height. However, this treatment was discontinued three months later. On June 11, 1935, the patient's height was 48 inches, her weight 57 pounds, her vision 6/9 in each eye, and her fields were full for the first time since she came under our observation. She reported for examination again October 5, 1935, at which time she was neurologically negative, vision 6/9 and fields full, height 48⅛ inches and weight 54 pounds, a loss of 3 pounds. Five or six days ago she had an occasional sense of nausea, particularly in the morning, but never vomited.

Briefly, there has been no recurrence of any symptoms since the cyst was tapped for the second time, June 11, 1934. Immediately after this, she received a course of roentgen treatment and has been free from recurrence ever since, that is, for a period of two and one-half years (see Figs. 4 and 6).

Discussion. Attention is called to the papilledema, to the headache, and to the vomiting, as indicative of the increased intracranial pressure. If the history of this case is read with care, it will be found to illustrate several points of practical importance. There seemed to be no question as to the diagnosis; the pituitary syndrome, in which amenorrhea and dwarfism were the outstanding symptoms, the area of calcification, signs of increased pressure, both general and focal, the field distortion and the papilledema, which one would anticipate did the tumor take its origin from the higher rather than the lower cell group. That the child did not regain normal height nor menstruation might well be anticipated when the damage to the pituitary body was of such long standing and beyond the time when recovery of function was likely to occur. It should be remembered that when the child was first seen she had not grown any for six years, nor had she menstruated for the same period.

The tendency of these tumors to become cystic is well illustrated by the following case, in which 210 c.c. of a semi-thick, yellowish green fluid was recovered from the cyst.

CASE II. *Summary.* A boy, aged ten, with a history of convulsions, fronto-occipital headache and loss of vision. Cyst evacuated through first temporal convolution followed by marked improvement. Recurrence of symptoms and cyst tapped on seven occasions subsequently; roentgen treatment instituted, and between December 26, 1934, and December 19, 1935, the boy received three series of roentgen treatments, for periods of ten, twenty-one and thirty days respectively since the completion of which he has remained in excellent condition.

J. S., male, aged ten (File No. 27261), was referred to the Neurosurgical Service by Dr. Karl Rothschild, July 12, 1933.

Present Illness. When two and a half years old the child developed an osteomyelitis following a fall on his knee. A year ago he had the mumps and during this a generalized convulsion. At first occurring every month, they occurred now more frequently. Two months ago he complained of fronto-occipital headaches. A month ago his mother noticed his vision was failing and he is now almost totally blind.

Family History. Mother has had four miscarriages.

Previous Medical History. Measles, chickenpox, pneumonia and influenza.

General Physical Examination. Negative.

Neurological Status. Slight left facial weakness; left homonymous hemianopia, vision, O. D. and O. S. 1/60 (Fig. 7), papilledema, O. S. plus 2, O. D. plus 4; roentgen signs of increased intracranial pressure.

Preoperative Diagnosis. Left frontal lobe tumor or craniopharyngioma.

Ventriculogram, July 17, 1933 (Dr. Rowe). About 5 c.c. in all drained from each side. After much coughing, moving of the head and occasional jugular compression, 8 c.c. of air was injected on each side. In the anteroposterior view a moderately enlarged right lateral ventricle could be seen pushed extremely to the left and upward. The third ventricle and apparently even the fourth were shifted to the left. In the lateral views there seemed to be a defect in the region of the middle fossa possibly pressing up from below (Fig. 8).

Operation, July 17, 1933. Craniotomy (Dr. Groff). Under avertin plus local anesthesia a large transfrontal skin flap and a somewhat smaller bone flap were made, exposing a small portion of the frontal, parietal, and all of the temporal lobes. The dura was extremely tense and it was necessary to administer 50 c.c. of 50 per cent glucose to reduce the tension. The dura was then reflected with the base toward the midline. The gyri of the temporal lobe and part of the frontal lobe exposed were wider than normal, but not discolored. There was a suggestion of fluid on palpation in this area. A cannula was therefore introduced at the anterior end of the first temporal convolution. This encountered resistance at a depth of 2 cm. and on further insertion entered a cyst cavity. From this cavity we were able to withdraw 210 c.c. of a semi-thick, yellowish green fluid which solidified on standing. This reduced the intracranial tension remarkably. The dural flap was sutured in place and the bone flap replaced. As the blood pressure had dropped below 60, the patient was given 400 c.c. of a 10 per cent glucose solution.

Before the patient was discharged, the cyst was tapped again (Aug. 23, 1933) and 50 c.c. of a typical motor oil fluid with cholesterin crystals removed.

Discharged, August 31, 1933.

First Readmission, October 15, 1933. *Interval Note.* Marked improvement since first admission; boy has begun to take an active interest in play and other boys; has had only one headache, a week ago today. He has an enormous appetite, wants to eat constantly and has become irritable. A month ago his eyesight began to fail.

Examination. Slight lagging left corner of mouth, slight asynergia left leg; vision, O.S. 3/60, O.D. 1.5/60 (Fig. 7), no choking, pupils irregular; roentgenograms show calcification in suprasellar region.

Operation, October 30, 1933 (Dr. Frazier). Original flap reflected. What we identified as the vessels of the Sylvian fissure passed obliquely upward at a rather sharp angle. The surface of the temporal lobe beneath this level was anything but normal in appearance. It was cystic on palpation. A cannula was introduced downward and forward but only a few drops of fluid escaped.

It was then decided to expose the cyst by elevating the frontal lobe, following the greater wing of the sphenoid bone and about half way down toward the optic foramen the capsule of the cyst ruptured and a large quantity of yellowish fluid with plenty of crystals escaped. By dividing the cyst wall along the margin of the sphenoidal ridge, we were able to secure ample exposure of the cavity of the cyst. The lining membrane was very uneven on the surface and appeared mostly encrusted. A portion of the cyst wall was removed for examination.

It was not thought wise to attempt to remove the entire lesion which filled the temporal fossa. As in the first operation, the boy's condition after the exploration was not very satisfactory either as to blood pressure or pulse. For that reason, too, we decided against any radical steps. While we were closing the wound the patient received 300 c.c. of blood by transfusion. Provision for decompression was made by removing one-third of the bone from the flap, and, in order to secure bony union, if

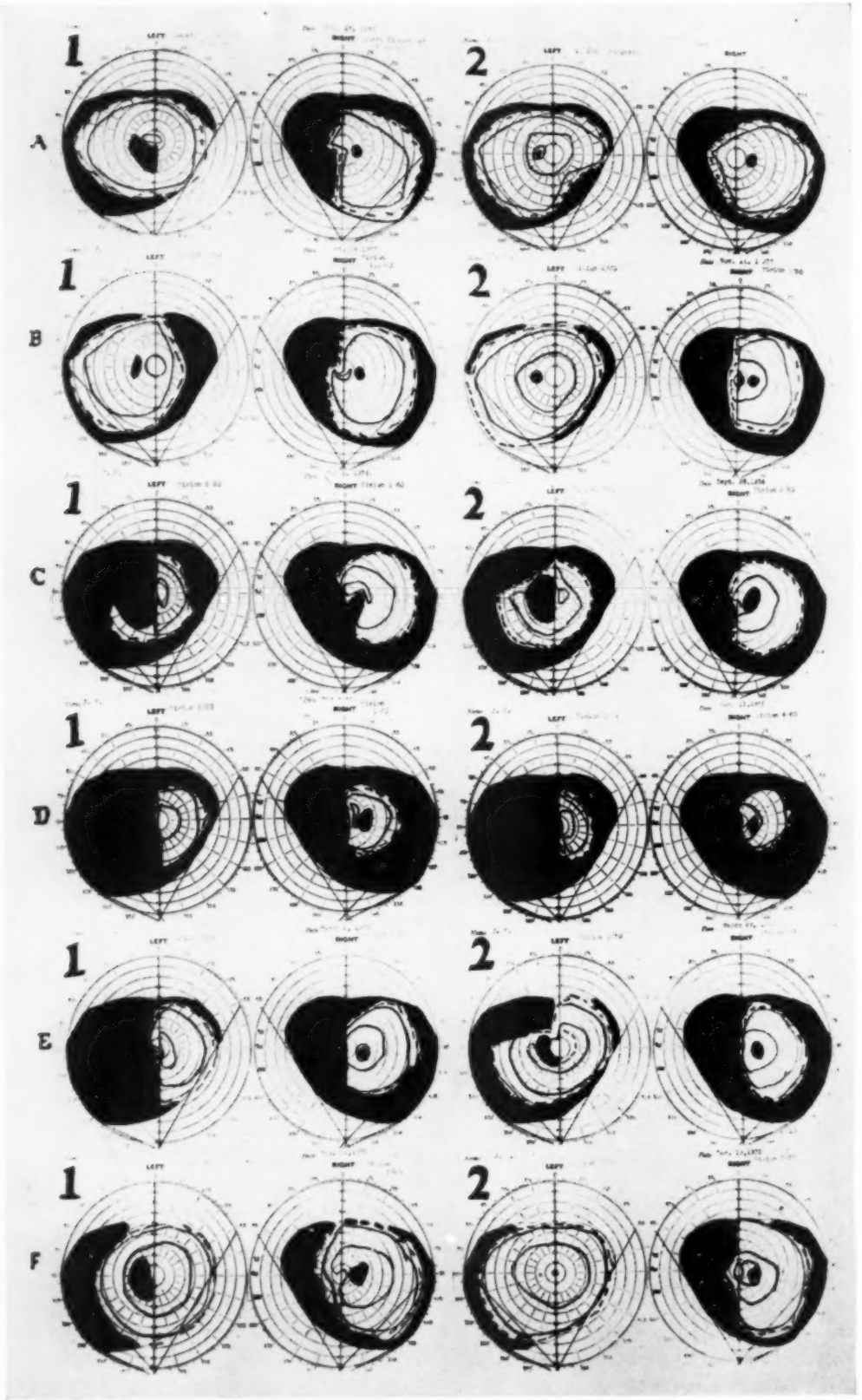


FIG. 7. Case II (*See opposite page*)

possible, on the right plane, three very fine silver wire sutures were introduced after the margins of the bony defect had been laid bare.

Discharged, November 13, 1933.

Follow-up Notes, April 17, 1934. Convulsions recurred. April 25, 1934. Since January generalized convulsions. For two weeks severe headache and for two days frequent vomiting; left hemiparesis; right oculomotor paralysis; flap tight.

Second Readmission, April 25, 1934. Since last discharge recurrence of convulsions and intracranial pressure; headaches; head appears to be getting larger.

Examination. Wasting of left arm and leg; discs yellowish white; gait unsteady; left dysdiadokokinesia; left temporal hemianopia; left facial weakness.

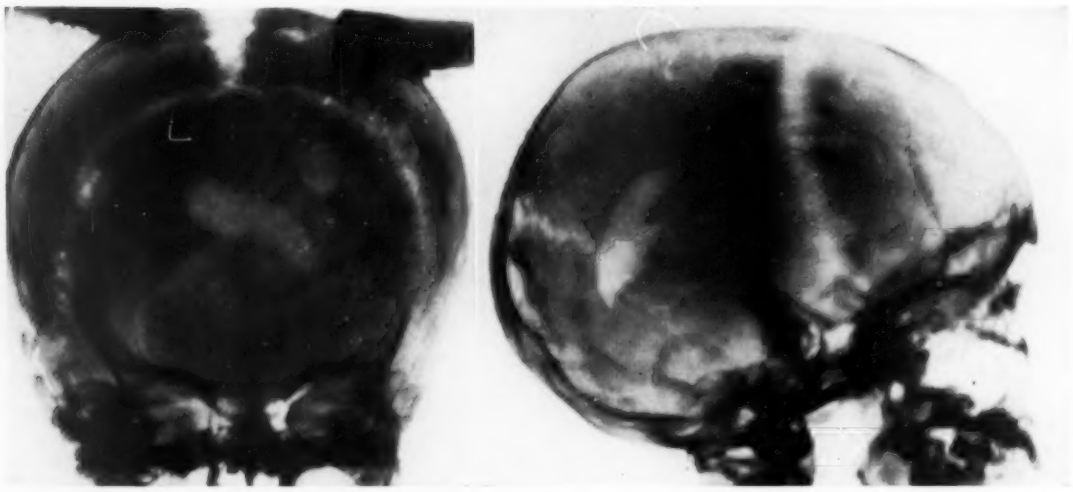
First Operation, April 30, 1934 (Dr. Frazier). Evacuated 200 c.c. from cyst and 20 c.c. of air injected. Roentgenogram shows outline of large loculated cyst in right temporal region.

Second Operation, May 23, 1934 (Frazier-Rowe). Scalp flap reflected, vertical incision in

Fig. 7. Case II.

		Date	Vision	Fields
A	1	July 13, 1933 Before first operation	O. S. counts fingers at 3″ O. D. counts fingers at 2″	Left homonymous defect, more marked in right field
	2	July 27, 1933 After first operation	O. S. 4/60 (fingers) O. D. 1/60 (fingers)	Left homonymous defect, much less marked
B	1	Oct. 24, 1933 Before second operation	O. S. 3/60 O. D. 1.5/60	Binasal field defect, more marked in right field
	2	Nov. 11, 1933 After second operation	O. S. 6/60 O. D. 1/60	O. S. practically full O. D. essentially unchanged
C	1	May 8, 1934 Before third operation	O. S. 5/60 O. D. 1/60	Large irregular left homonymous defect with some generalized contraction
	2	Sept. 26, 1934 Four months after third operation.	O. S. 6/30 O. D. 6/60	Very definite improvement, particularly in left field
D	1	Dec. 13, 1934 Before first course x-ray	O. S. 6/60 O. D. 1/60	Left homonymous hemianopsia with generalized contraction, particularly on right
	2	Jan. 11, 1935 After first course x-ray	O. S. 6/60 O. D. 4/60	Still further contracted despite operation
E	1	March 5, 1935 Before second course x-ray	O. S. 6/60 O. D. 6/60	Left homonymous hemianopsia, slight generalized contraction, particularly on right
	2	March 28, 1935 After second course x-ray	O. S. 6/30 O. D. 5/60	Marked improvement in temporal field on left
F	1	Nov. 21, 1935 Before third course x-ray	O. S. 6/30 O. D. 6/60	Moderate left homonymous defect and enlargement of blind spots
	2	Dec. 19, 1935 After third course x-ray	O. S. 6/60 O. D. 6/60	Marked improvement in left field and reduction in size of blind spots

Note: Outer solid line, field for 1° white objective; broken line, field for 2° white objective; inner solid line, field for 1° red objective.



A *B*

FIG. 8. Case II. *A*. Ventriculogram, anteroposterior view, showing moderately enlarged right lateral ventricle, pushed extremely to the left and upward *B*. Ventriculogram, lateral view, showing defect in both lateral ventricles, indicating a lesion in the middle fossa probably pressing up from below.

temporal muscle, introduction of cannula and evacuation of cyst.

Transcortical incision into cyst cavity. Cavity smaller, now only size of walnut. Section of wall removed for examination and wound closed; 210 c.c. 2 per cent glucose intravenously.

Discharged, June 10, 1934.

Third Readmission, December 11, 1934. No essential change in condition except return of vomiting. Cyst evacuated December 24, 1934, and January 9, 1935.

Treatment. Roentgen therapy begun December 31, 1934, to January 9, 1935. Tumor dose: 1,371 r; period of treatment ten days.

Discharged, January 16, 1935.

Fourth Readmission, March 4, 1935. Patient in excellent condition; no convulsions; vision O.D. 6/60, O.S. 6/60. Now in third grade at school (Fig. 7).

Treatment. Roentgen therapy, second series, March 5, 1935, to March 26, 1935. Tumor dose: 2,032 r; period of treatment twenty-one days.

Discharged, April 1, 1935.

Fifth and Last Readmission, November 19, 1935. Patient in excellent condition; no convulsions; vision O.D. 6/60, O.S. 6/30 (see Fig. 7).

Treatment. Roentgen therapy, third series, November 19, 1935, to December 19, 1935. Tumor dose: 3,464 r; period of treatment thirty days.

Discharged, December 19, 1935 (see Fig. 9).*

Discussion. As for those tumors which take their origin from the lower anlage, Figure 10, is a diagrammatic sketch, in every respect typical, showing the relationship of the tumors which take their origin from the lower group of cells. Note the relationship of the tumors to the chiasm, and, more particularly, to the third ventricle. In this particular case, the third ventricle is not encroached upon, there are no signs of intracranial pressure, the optic atrophy is primary, not secondary, and the field distortion either is bitemporal or an homonymous hemianopsia.

SURGICAL CONSIDERATIONS

To one who has had a large experience in dealing on the operating table with tumors in this location, the difficulties attending any attempt at radical removal at once suggest themselves. So let us at this juncture focus our attention on these problems. Not only are there definite obstacles and difficulties attending attempts at removal but there are definite dangers as well. Wherefore, let us bear in mind

* This patient again returned because his mother thought his vision was still failing. On June, 3, 1936, the left field showed a superior temporal cut which completely disappeared after another series of irradiation.

these two surgical factors: on the one hand, difficulties, and on the other, dangers. The causes thereof are so intimately related that they may well be considered together. In the first place, let us bear in mind that on the wall of the third ventricle there are important centers and perhaps the most important those which have to do with temperature regulation. The possibility of hyperpyrexia as a postoperative complication, and perhaps a fatal one, must be borne in mind.

Any plan of treatment which carries with it as an essential part of its program the radical removal of the lesion itself is destined to failure in the first place because of the high mortality rate. And since it so happens in many instances that the tumor may be only relatively malignant, and by a process of cystic degeneration may gradually disappear, it becomes necessary, if not almost mandatory, to adopt a plan essentially free from risk.

Fig. 9. Case 11. Photograph of patient, March 11, 1936, two years and eight months after treatment was begun; note absence of any protrusion at site of operative decompression.

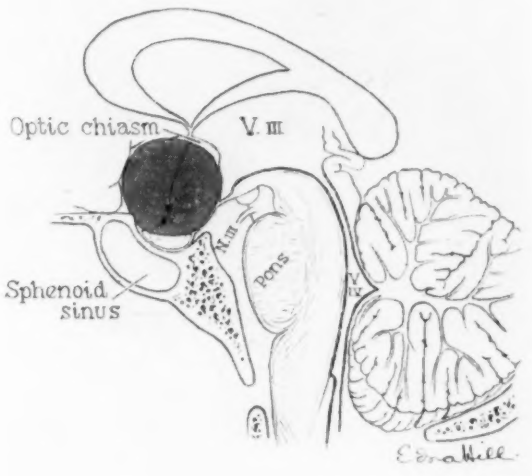


Fig. 10. Hypophyseal stalk tumor arising from lower rest eroding the sella, compressing the optic chiasm and nerves.

In many of the cases reported, the treatment in general has been an attempt at exposure with evacuation of the cystic contents, and an attempt—as most of these tumors are cystic—at partial removal of the cyst wall.

However, with the evacuation of the cyst the battle is only half won since in the majority of cases the cyst will refill and all the symptoms, both local and general, will recur. It is at this juncture that the modification of the plan of treatment we propose is introduced, namely, the exposure of the cyst wall to irradiation. It is assumed that the reaccumulation of fluid is due to the activity of these peculiar cells lining the cyst wall and it was with the understanding that the activity of these cells might be arrested by irradiation that the treatment was first undertaken. The following is a case which illustrates, in many particulars, the points we are now discussing:

Case III. *Summary*. In a boy, aged fourteen, with a history of headache, vomiting, vertigo, and tinnitus of two months' duration, signs of pituitary dysfunction and suprasellar calcification, an exploratory craniotomy finds excessive

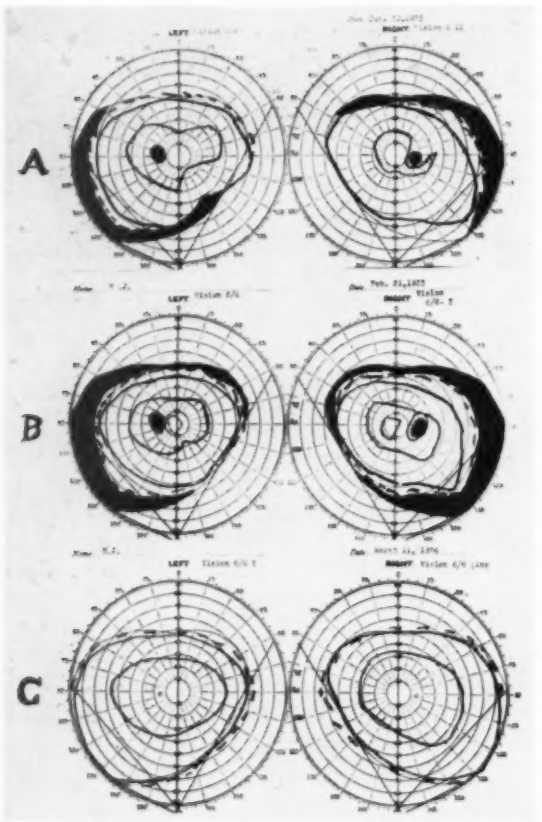


FIG. 11. Case III. *A.* January 30, 1933. Before operation: vision, O. S. 6/6; O. D. 6/12. Fields: slight bitemporal defect. *B.* February 21, 1933. After operation: vision, O. S. 6/6; O. D. 6/6–3. Fields: slight bitemporal defect. *C.* March 11, 1936. Three years after operation: vision, O. S. 6/6; O. D. 6/6 plus. Fields: full.

pressure, but no tumor can be seen. Operative diagnosis, hypophyseal stalk tumor. Following a decompression and course of roentgen treatments, the patient remains symptom-free at last examination.

H. J., male, aged fourteen (File No. 26135), was referred to the Neurosurgical Service of the University Hospital by Dr. A. L. Sherk, with a chief complaint of headache. Admitted January 27, 1933.

History of Present Illness. December 1, 1932, about two months ago, the patient began to complain of headaches, not constant, but recurring at frequent intervals. Eight days after onset of illness he noticed a blind spot in the center of vision of his right eye. December 20, 1932, he vomited and was unable to retain food for two days and January 13, 1933, he complained of dizziness.

Family and Previous History. Inconsequential.

General Physical Examination. Negative.

Neurological Status. Signs of pituitary dysfunction (thin skin, adiposity, infantile genitalia, scanty hair, tapering fingers, B.M.R. minus 15); vision O. D. 6/12, O. S. 6/6, papilledema O. S. plus 2.5 (Fig. 11), O. D. plus 3.5; bilateral enlarged blind spots; nystagmus, slight horizontal to right and left; hearing, right ear 13.8 per cent, left ear 14.5 per cent; anosmia right and left.

Roentgen Examination. Erosion dorsum sellae and posterior clinoid processes. Suprasellar calcification (Fig. 12).

Operation, February 10, 1933 (Frazier). Transfrontal craniotomy, right, avertin anesthesia, subtemporal decompression.

There was some uncertainty as to whether or not the tumor was in the posterior fossa, and in order to eliminate this as a possibility, cannulas were introduced into the posterior horns of the ventricles and after ten or fifteen minutes not more than 5 or 10 c.c. altogether had escaped, mostly from the right ventricle. We assumed from this that there could not be a posterior fossa tumor, that the ventricles could not have been dilated, saw no necessity for a ventriculogram, and at once proceeded to carry out the transfrontal exploration on the right side.

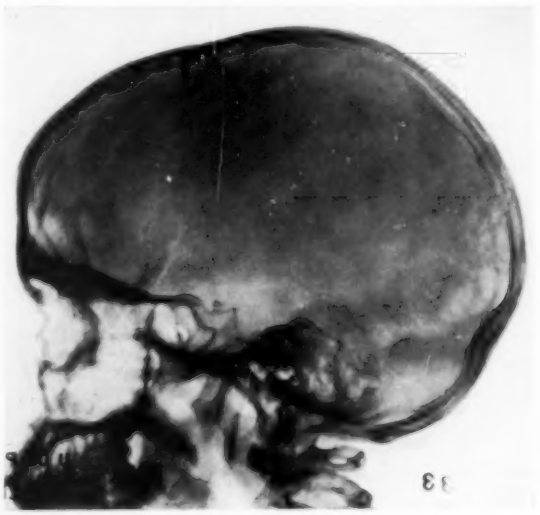


FIG. 12. Case III. Roentgenogram showing erosion of the dorsum sellae and posterior clinoid processes; suprasellar calcification.

A flap was reflected by the dual method. The frontal sinuses were not enlarged so that the anterior margin was just above the supraorbital ridge. When the bone flap was reflected it bulged considerably above the dural level. This convinced us at once that we were dealing with an extrasellar lesion and a ventricular block.

Accordingly, we proceeded to tap the anterior horn of the right ventricle, at the same time giving 75 c.c. of 50 per cent glucose. This proved most effective and the cerebral hemisphere became flush with the dural margins.

After rongeuring away bone from beneath the temporal muscle so as to give us a lower approach, we proceeded, as is our custom in pituitary explorations, to elevate the frontal lobe following the course of the greater wing of the sphenoid bone. As we did this considerable fluid escaped from the base and the basal cisterns. In order to allow as much of this as possible to escape, we proceeded leisurely until we reached finally the right optic nerve. By using such pressure as was thought permissible, the right and left optic nerves and the anterior rim of the chiasm could be seen but we could not see behind the chiasm and no tumor presented in front.

From this observation we were of the opinion that we were dealing with a tumor of the craniopharyngeal duct, high up, behind the chiasm, in a position which we have heretofore believed to be unapproachable with any reasonable degree of safety.

Consequently, we were content with this exploration, made provision for liberal decompression by removing all the bone from under the temporal muscle, and then closed the wound. The galea in this case was very tense and, in attempting to suture it, the sutures tore through in many places so that we decided to use a through and through suture and leave the galea sutures out.

The patient's condition was surprisingly good throughout the operation. He required no stimulation of any kind. His blood pressure at the conclusion of the operation was about what it was in the beginning and we saw no reason for fluids or stimulation or blood.

Operative Diagnosis. Hypophyseal stalk tumor.

The patient was discharged February 21, 1933, and arrangements made for a course of roentgen treatment (Fig. 13).

November 10, 1933, eight months after discharge, the following note was made on his

Fig. 13. Case III. Photograph of patient ten days after operation, showing well-healed scar.

"follow up" record: "His headache and vomiting have completely disappeared; his vision is 6/6 in each eye; his fields are practically normal; roentgen examination shows no change from that made before the operation; the site of the decompression is soft, showing that now there is no increase in intracranial pressure as there was before the operation. For the time being, therefore, we must consider the patient symptom-free. The only condition which might call for treatment is the excessive weight. He has gained about 20 pounds since his operation and his height is a little below normal.

Treatment. Roentgen therapy November 13, 1933, to December 14, 1933. Tumor dose: 2,743 r; period of treatment thirty-one days.

Roentgen therapy March 20, 1934 to April 19, 1934. Tumor dose: 2,743 r; period of treatment twenty-nine days.

January 2, 1935. Almost two years after discharge, the follow-up note says: "Entirely normal, returned to school, A's in all subjects, getting fatter, slight optic atrophy, general neurological examination negative."

*February 19, 1936.** Three years after dis-

* At the last follow-up (Nov. 8, 1936) the patient has had no recurrence.

FIG. 14. Case III. Photograph of patient three years after operation.

charge, the neurological examination was essentially negative. Hand fields normal (Figs. 11 and 14).

CASE IV. This case is quite similar to Cases I and II and therefore only a brief outline of her findings is included.

A girl, aged eleven, with signs of impaired vision, headache and nocturnal enuresis. Her hypophyseal stigmata consisted of widely spaced teeth and hypertrophied tongue.

Roentgenograms showed suprasellar calcification with erosion of the dorsum sella.

Visual fields showed a bitemporal hemianopsia.

Operation, April 24, 1934, evacuation of 40 c.c. of yellowish fluid containing cholesterin crystals.

June, 1934. Six weeks after the evacuation there was a recurrence of symptoms.

July 26, 1934. The cyst was again evacuated by Dr. Frazier.

August, 1934. A series of irradiation was given which was followed by improvement in the visual fields. The patient remained well until December, 1936, when she had another recurrence. We have been unsuccessful in getting her back for another series of radiation therapy.

DISCUSSION OF IRRADIATION EFFECTS

The hypophyseal stalk tumors have been considered by most radiologists to be resistant to roentgen therapy. The American literature on the subject is unsatisfactory since most of the reports concern unverified cases which have, for the most part, been unresponsive to therapy.

From the microscopical structure, these tumors would appear to be radioresistant. Composed, as they are, of mature epithelial cells and stroma which is only moderately vascular, one would not be inclined to anticipate a good response to roentgen therapy. However, radiation therapy is a comparatively young science. As we learn more about the proper technique of delivering this form of therapy and more about the quantity of radiation that can safely be tolerated, we also learn more about individual cell sensitivity. Broders'[2] classification, while it presents an excellent working basis for the prognosis in radiation therapy, is not by any means an inviolate rule in actual practice. Furthermore, experience has led us to believe that cell secretion may be inhibited without cell destruction. The evidence in favor of this has been our observations of the effect of irradiation on the secretion of glandular tissues, particularly the thyroid and salivary glands. This fact alone may explain the beneficial effects of roentgen therapy in the cases of stalk tumor presented in this paper.

If we are to obtain definite results here or in other fields by irradiation, we should adopt a technical arrangement which can be reproduced.

The analysis of all irradiation data should be made on the basis of three fundamental factors: namely, the quantity of radiation, the quality of radiation, and the time element.

The quantity of radiation is best expressed as tumor dose in roentgens. In

TABLE I

SHOWING TUMOR DOSE, THE DOSE PER SERIES, THE DISTRIBUTION AND THE TIME INTERVAL

Case	No. of Series	Dose per Series	Tumor Dose	Distribution of Portals	Duration of Treatment	Average interval between Series
I	1	1,600 r×3	2,844 r	Each lateral, vertex	47 days	—
II	3	(1) 800 r×3	1,371 r	Each lateral, vertex	10 days	
		(2) 1,600 r×2	2,032 r	Each lateral	21 days	5 months
		(3) 1,600 r×4	3,464 r	Each lateral, vertex, forehead	30 days	
III	2	(1) 1,600 r×3	2,743 r	Each lateral, vertex	31 days	3 months
		(2) 1,600 r×3	2,743 r	Each lateral, vertex	29 days	
IV	1	1,040 r×3	1,782 r	Each lateral, vertex	11 days	

Table 1 we have also indicated the total radiation, measured in air, that was delivered to each portal at any one series. All portals were 8 by 10 cm., the scattered radiation being 27 per cent. The depth dose at 7 cm. is 50 per cent and at 8 cm. 40 per cent (tables of Weatherwax[6]). In the calculation of the tumor dose, we did not consider the exit radiation.

The equipment used consisted of a single Le Tour circuit operating at 165 kv., constant potential, 15 ma. current. All of the patients were treated at 50 cm. skin target distance with 0.5 mm. Cu and 2 mm. Al filtration. The half-value layer with this equipment is 0.88 mm. Cu, and the effective wave length 0.17 Å.

In this series the therapy was delivered according to the divided dose method. Patients were treated daily or on alternate days. The daily dose varied with the response of the individual. Whenever possible we attempted to deliver 200 r (measured in air) to each of two portals at one sitting. To do this, it has been found advisable to begin treatment with a small dose (50 r), using a daily increment of 50 r as long as the patient shows no radiation sickness or evidence of increased intracranial pressure. The average duration of each series was three to four weeks, depending upon the number of portals utilized and the quantity of radiation delivered through each portal.

Thus it will be seen that following these exposures, this dosage and in general this technique in the 4 cases herewith reported, the patients have gone twenty-three,

TABLE II

RESULTS IN EIGHT CASES TREATED BY SURGERY ALONE

Case	Treatment	Vision	Visual Fields	Other Symptoms	Results
1	Decompression and evacuation	1 plus	2 plus	Same	Fair condition 2½ years after operation
2	Subtotal removal	—	—	—	Death 3 years after operation
3	Subtotal removal	—	—	—	Death 2½ years after operation
4	Subtotal removal	—	—	—	Death 9 months after operation
5	Attempt at exposure	—	—	—	Death 3 months after operation
6	Decompression	—	—	—	Death 2 months after operation
7	Partial removal	—	—	—	Death 1½ months after operation
8	Attempt at removal	—	—	—	Death at operation

TABLE III

SHOWING THE INTERVALS BETWEEN ASPIRATIONS AND THE AVERAGE LENGTH OF TIME BETWEEN ASPIRATION AND FIRST EVIDENCES OF RECURRENCE BEFORE ROENTGEN THERAPY WAS INSTITUTED

Case	Period under Observation	Dates of Operation	Aspiration of Cyst	Time Interval between Recurrence and Previous Tapping
I	March 2, 1934 to May 1, 1936 (25 mo.)	March 10, 1934. Exploratory craniotomy. Cyst found and evacuated	(1) March 10, 1934 (2) June 11, 1934	8 wk.
II	July 12, 1933 to May 1, 1936 (34 mo.)	July 17, 1933. Exploratory craniotomy. Cyst found and evacuated	(1) July 17, 1933 (2) Aug. 23, 1933 (3) Oct. 30, 1933 (4) April 30, 1934 (5) May 23, 1934 (6) Dec. 24, 1934 (7) Jan. 9, 1935	8 wk. 10 wk. 3 wk. 6½ mo.
III	Jan. 27, 1933 to May 1, 1936 (39 mo.)	Feb. 10, 1933. Exploratory craniotomy. Solid tumor; no cyst		No recurrence
IV	April 12, 1934 to May 1, 1936. (24 mo.)	April 24, 1934. Exploratory craniotomy. Cyst found and evacuated	(1) April 24, 1934 (2) July 26, 1934	6 wk.

TABLE IV

SHOWING PERIOD OF ROENTGEN TREATMENT; VISION BEFORE OPERATION AND AT LAST FOLLOW-UP; TIME INTERVAL WITHOUT EVIDENCE OF RECURRENCE SINCE FIRST ROENTGEN THERAPY

Case	Roentgen Treatment	Vision	Time Interval without Evidence of Recurrence Since First Roentgen Therapy
I	May 21, 1934, to July 7, 1934	Before operation: O. S. and O. D. 6/12+ Last follow up: O. S. and O. D. 6/6	30 mo.
II	Dec. 31, 1934, to Dec. 19, 1935	Before operation: O. S. counts fingers at 3″ O. D. counts fingers at 2″ Last follow up: O. S. 6/60 and O. D. 6/60	17 mo.
III	Nov. 13, 1933, to April 19, 1934.	Before operation: O. S. 6/6 and O. D. 6/12 Last follow up: O. S. 6/6 and O. D. 6/6	39 mo.
IV	Aug. 3, 1934, to Aug. 14, 1934	Before operation: O. S. 6/60 and O. D. 6/30 Last follow up: O. S. 6/22 and O. D. 6/22	20 mo.

seventeen, thirty-nine and twenty months respectively without any signs of recurrence. From this we may assume with reasonable assurance that the process has been arrested or that no longer is there any secretory action in the epithelial cells lining the cysts.

All of these 4 patients have returned to active life; they are attending school and carrying on all activities quite normally. In Case III, there was a small tumor that could not be exposed, but clinically and roentgenographically presented all the characteristics of a hypophyseal duct tumor. In the other cases the tumor was exposed during the initial surgical procedure. Previous to starting roentgen therapy, these cases had required several aspirations of fluid as it reaccumulated, producing a return of symptoms and regression of visual fields and vision. Since using such therapy, aspirations have not been required. Table II shows the intervals between aspirations and the average length of time between aspiration and first evidences of recurrence before roentgen therapy was instituted.

RESULTS

Of 8 cases of hypophyseal stalk tumor, treated by surgery alone (see Table II) 1 died at the time of operation, 3 within three months of the operation, 1 within nine months and 3 within three years of the operation. Of the entire series, *only 1 was alive and in fair condition thirty months after the operation*. Compare these figures and results with those in the 4 cases treated by irradiation and aspiration who were alive and well on an average of thirty and a half months after treatment was instituted. In these 4 cases, compare the short period of time between aspiration of the fluid and return of symptoms, before irradiation, with the comparatively long interval of freedom from symptoms following the first roentgen treatment (Tables III and IV). In 1929, Beckmann and Kubie[1] reported 21 cases, all operated upon, *17 of which died shortly after the operation*, and the 4 surviving showed little or no improvement.

From our experience with these lesions, it would seem reasonable to assume in many instances that the symptoms are due to the filling and refilling of the cyst and if any conclusions at all can be drawn from our experience with this series of 4 cases, we must assume that the tendency for the fluid to reaccumulate is decreased by irradiation. We admit that 4 cases is a small number from which to draw conclusions. On the other hand, it is better sometimes to draw conclusions from a small number of cases, which, as in this instance, have been subjected to a most critical analysis.

CONCLUSIONS

We submit for consideration a method of dealing with a lesion we have designated as "hypophyseal stalk tumor." The essential feature of this treatment is its freedom from risk. We recognize that any attempt at radical removal of the lesion is essentially attended with risk and may well be fatal in its outcome. Such is true of any radical operation which has as its objective the removal of any portion of the wall of the third ventricle or of any radical steps in this location.

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ROENTGEN THERAPY IN ACUTE PARA-ARTHRITIS*

By ALFRED A. DE LORIMIER, M.D.
Captain, Medical Corps, United States Army
ANCON, CANAL ZONE

INTRODUCTION

A MANIFOLD nomenclature has developed for description of a group of "itises" or "algias" which we find located in the neighborhood of various joints. The literature is now so complicated in this field that it has become necessary, when speaking of the condition, to include mention of synonymous terms which have been used by various observers or to explain the inclusion of a number of so-called entities. The group to be discussed will not include lesions located actually within a joint but rather those closely related conditions of the regional tissues which are so often blanketed with such terms as "myofascitis," "tendinitis," "fibrositis," "bursitis," or even "neuritis" and "myalgia," to which may be attached a proper name or a combination of them. The symptom-complex is a fairly common one and it is found in various parts of the body. Our interest, however, has been limited to those very painful, crippling, more or less limited lesions which may involve one or another part of the extremities. For the present consideration we have selected cases which not only have manifested clinical indications as to this condition but in which, moreover, there has been roentgenological support as to the diagnosis. We have attempted to locate the site of pathology in terms of the actual tendon or muscle bundle and to study the most effective method of radiation therapy.

The shoulder appears to be the most frequent site for this type of involvement. In this region, the condition is commonly called "bursitis." Some writers have been more specific, applying the prefix "subacromial" or "subdeltoid." In fact, descriptions of one or the other of these captions became so numerous that in more recent writings, Carnett,[6] Mumford and Martin,[21] and others, have found it necessary to explain that these two terms refer to one and the same bursa. Codman[9] has described wide ramifications of this bursa but he believed that bursal irritation, if present, is secondary to the changes beneath the bursal wall or within the regional tendons. When calcareous deposits were found at operation they were usually associated with the tendon of the supraspinatus. Carnett[7] likewise excluded the bursa saying that the "deposit is always outside the bursa." The reasons for implicating this bursa can probably be attributed to the very early descriptions, in 1907, by Painter[23] and Baer.[2] These observers were probably the first to note the presence of concretions in some of these cases and at that time they located the deposits within the sac. Hitzrot[18] reported a case, apparently representing the exception, in which "rice bodies" were definitely located within the bursa.

Similar changes are occasionally seen in the hip. With acute symptomatology here, the condition is likely to be dismissed as a "sciatica." Literature concerning changes in this location appears to be sparse, though Goldenberg and Leventhal[14] have recently described concretions within the tendon of the gluteus medius or its regional bursae.

Much has been written concerning concretions about the knee. With acute symptomatology, the condition is likely to be called "Pellegrini-Stieda's disease." "Stieda's shadow fracture," or "Köhler-Pellegrini-Stieda concomitant shadows," etc. The deposits have been located in the region of the internal lateral ligament or in the tendons of the adductor magnus or vastus medialis.

Similar findings may occur in the elbow region or the tendons about the smaller joints of the hands or feet. In most of these cases the joint itself is spared; the

* From the Department of Radiology, Gorgas Hospital, Ancon, Canal Zone.

condition is characterized by changes which are limited to a sector of the tissues peripheral to the joint—thereby invoking the term "para-arthritis" as suggested by Odessky.[22]

ETIOLOGICAL CONSIDERATIONS

Trauma, of one sort or another, appears to be the most frequently associated factor. Certainly in the region of the knee, and in many of the shoulder cases, these changes can be attributed to some single insult or to repeated injuries incident to work or play.[4,12] Codman[9] has considered "traumatic rupture" of fibers of the muscle or tendon as basic to the changes seen in the shoulder. Carnett[7] referred to the pathological studies of Case and Moschowitz who described a tendinitis with multiple small foci of necroses and calcifications. They attributed these changes to the million fold occupational traumata incident to pinching of the supraspinatus tendon between the grip of the humeral head and the acromial process or coracoacromial ligament. Similar traumata would readily be considered in the so-called "tennis elbow" or "occupational hip." The smaller joints of the extremities and therefore the regional tendons are likewise subject to repeated strains and injuries.

Factors other than injury must also be considered since this condition is found about equally among those of sedentary habits and those of great physical activity. Moreover, an individual showing involvement in one region is likely to show roentgenographic evidence or, at some time, clinical manifestations of the condition elsewhere. Particularly in such cases the possibility of a systemic factor must be considered. Pemberton,[24] Wyatt,[29] and others, have emphasized the relationship of stagnation of toxins. These might be of catabolic nature or assimilated from some focus of activity. Albee[1] believed that "in ninety per cent of cases of myofascitis, the toxic absorption is primarily from the colon; in the remaining ten per cent from teeth, tonsils, sinuses, often with secondary toxicity of the colon." It seems rational to believe that the effect of toxins would be increased in cases of hypotension and particularly in parts where deficiencies of circulation might result from injury, chilling, etc. In the tropics, acute flareups of activity are most numerous during the "dry season" when the heat is most noticeable and when local chillings result more readily because of the winds or because of the injudicious use of electric fans. Patients frequently volunteer information of having been in some type of draft or exposed to chilling.

Various other systemic factors have been considered. Llewellyn[20] stated that these patients show basal metabolic rates either of the lower limits of normal or below normal. Deficiencies in carbohydrate tolerance have been considered.[24] Such disturbances of metabolism would have greater deleterious effects in cases of hypotension and particularly in those parts having a relative deficiency in circulation, i.e., where there is a circulatory stasis.

SYMPTOMATOLOGY

During phases of acute inflammatory reaction, these lesions are accompanied by extreme aching pains. In many instances calcareous deposits have been found at the very onset of symptoms. They may be found about joints where no symptoms had been noted. Therefore in some cases, at least, their development would seem to antedate the episodes of pain. Nevertheless it appears that they bear a relationship to the chronicity of symptoms because when they are present it is so common to hear that most insignificant injuries or exertions suffice to excite flareups of crippling episodes. Moreover, between such episodes, when these concretions are present, there appears to be a greater incidence of dull pain, stiffness and limitation of joint motion. It would seem that the deposits act as mechanical irritants.

The pains may have a widespread distribution. For this reason, definite localization of the pathology might seem quite obscure. In the shoulder cases, for instance, though the nidus of activity is

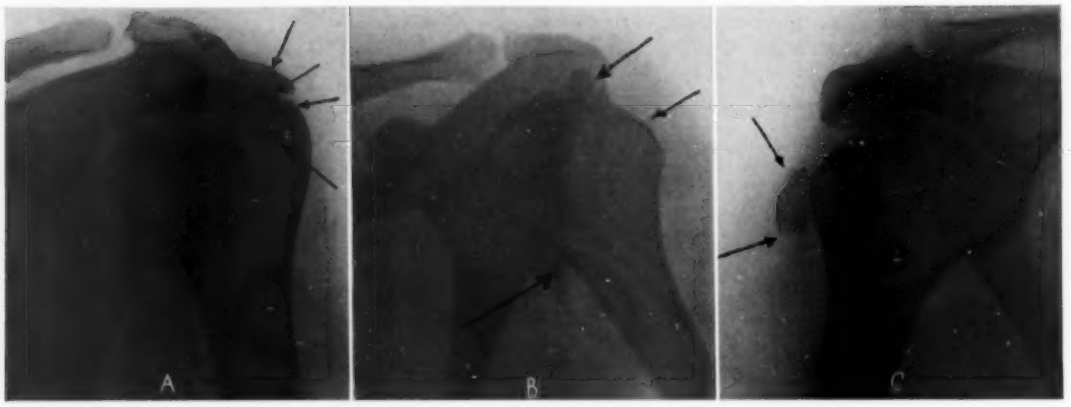

Fig. 1. Roentgenograms showing variation in the location of deposits in the shoulder. Stereoscopic studies in the case, *A*, showed these deposits to be intimately associated with the tendon of the supraspinatus, and to a lesser extent, with that of the infraspinatus. Note that this is a true anteroposterior projection and that these deposits are projected above the anterior portion of the tuberosity. Stereoscopic studies in *B* showed deposits in the region of the supraspinatus, the infraspinatus and the belly of the triceps brachii. In the first two, note that this projection was made with internal rotation of the extremity and that the deposits appear to be located more posteriorly in *B* than in *A*, in relation to the ridge of the greater tuberosity. In *C*, this large deposit was located in the tendon of the teres minor. Note that it has been projected by internal rotation of the extremity and is in close proximity to the very posterior portion of the tuberosity.

usually in the tendon of the supraspinatus, the patient is likely to complain of having the most intense pains in the region of the insertion of the deltoid or upward into the lower cervical region, or perhaps down to the elbow or even to the finger tips following either the radial or ulnar nerve distribution. One might be inclined to think of an anginal syndrome. Many cases are considered to be a "brachial neuralgia." The pains of a para-arthritis are distinguished by their intensification during specific motion of the part. In the case of the shoulder, anteroposterior motion may well be tolerated, whereas abduction or rotation of the arm should quickly elicit the characteristic pains. With involvement about the hip, Lasègue's sign should serve to distinguish a true sciatica, whereas the para-arthritic would complain of pains about the hip when attempting to abduct or circumduct the thigh. For the smaller joints, the pains are similarly noted with stress or contraction of the particular muscle.

In many instances these pains become sharp and lancinating. They may prevent sleep and even the minimal jolting of motion in bed may be sufficient to cause these patients to cry out in anguish for relief. Ordinary analgesics may be ineffectual during these acute stages, and it may be necessary to administer codeine or morphine.

DIAGNOSIS

The symptoms of the condition are usually out of proportion to the clinical findings. Externally, the region may appear entirely normal with no evidence of swelling or of superficial inflammation. Cases of long standing may show atrophy of the involved muscle and even of neighboring groups, due to the guarding and relative disuse. As mentioned, the relation of pain to particular types of motion by the patient is most informative. Passive motion by the examiner, if productive of strain upon the involved muscle or tendon, should further indicate the location of the trouble. Palpation may elicit point tenderness over the site of maximum involvement; for instance, in the shoulder cases, when the supraspinatus is concerned, the site of tenderness is characteristically at the anterolateral border of the acromion,

whereas when the tendons of the infraspinatus or teres minor are involved, this point tenderness is likely to be more posteriorly located—just lateral to the outer border of the spine of the scapula; in cases of hip involvement, this tenderness can usually be elicited with deep pressure just posterior to the greater trochanter. Localization of tenderness in cases of the more exposed joints of the extremities can be expected to be even more clear-cut. These findings are seldom accompanied by any evidence of systemic effect. The temperature is likely to be normal or below normal and no blood changes should be expected.

Roentgenography offers the most convincing proof of the diagnosis. This is especially true in the cases showing calcareous deposits. It is important that special technique be used for these cases in order to expose deposits which might otherwise be masked by overlying skeletal densities. Stereoscopic studies are especially to be recommended for, by third dimensional projection these concretions can be more easily distinguished from fleckings or skeletal condensations, and identified as deposits in a particular tendon sheath or fascial space. In lieu of this procedure, it is important that exposures be made through several planes. Anteroposterior and lateral projections are usually feasible. In the case of the shoulder this can be accomplished by positioning the forearm first in external rotation and then in extreme internal rotation. In making these projections it is important that the target of the roentgen tube be so aligned as to project the widest possible spacing between the densities of the acromial process and the head of the humerus. To obtain this, the tip of the coracoid process might be taken as a landmark and the center of the target positioned 1 inch mesially and 1 inch cephalad, tilting the target downward and laterally about 10 degrees, when using a 30 inch focal-film distance. Similar considerations should be given the hip. Here stereoscopic projections are especially desirable, but when there is insistence upon flat films, the regions about the great trochanter can be exposed by using the same technique as in the shoulder cases, making one exposure with the maximum of internal rotation of the thigh, and another with the greatest possible external rotation. The target should be aligned to a point midway between the anterior superior spine of the ilium and the symphysis pubis. In other regions, comparable rotation films may be necessary. In some cases, without concretions, the condition may be recognized as a localized tendinous or fascial edema. To substantiate this evidence, contralateral comparisons may be necessary.

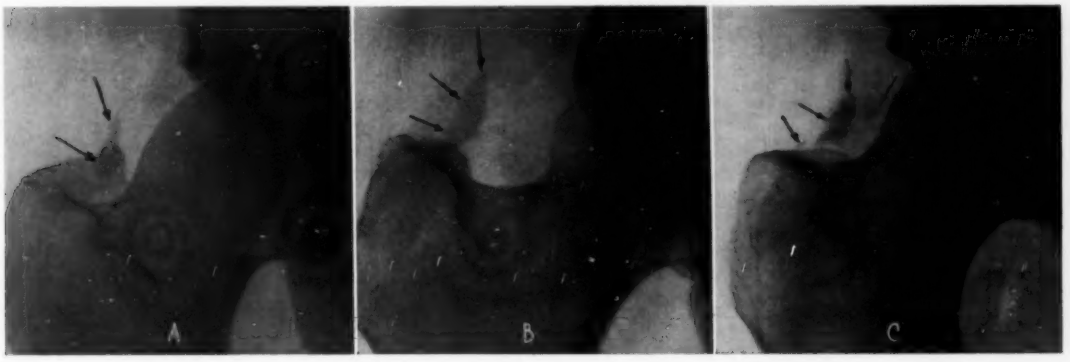

Fig. 2. Roentgenograms showing the appearance of calcareous deposits in the hip, as visualized on the flat film. Steroscopically, the deposit shown in *A* was projected to the very posterior plane of the insertion of the gluteus medius; in *B* the concretions appeared to be in the region of the insertion of the piriformis while in *C*, depth projection visualized the deposits in the planes of both the piriformis and the obturator internus. Note the variation as to density of these deposits. In all of these cases there was a striking and lasting relief of symptoms and complete absorption of the deposits after roentgen irradiation.

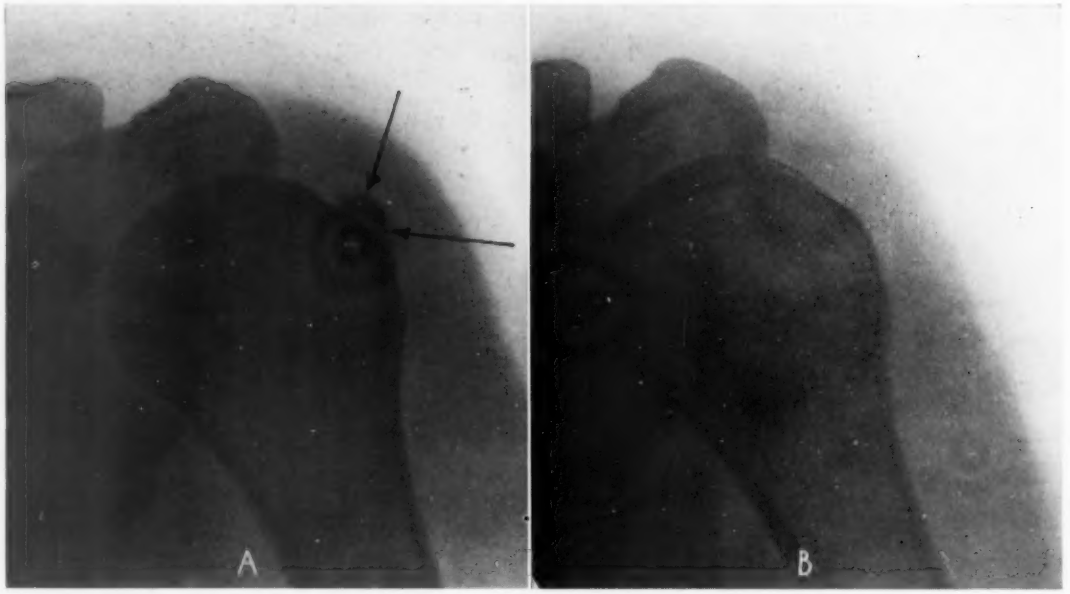

Fig. 3. Visualizing, *A*, a deposit in the region of the tendon of the infraspinatus as found before radiation, therapy, and, *B*, the appearance four weeks after this treatment. The patient (J.Y.) came into the clinic carefully guarding against motion of her left upper extremity, carrying the forearm in a sling, supporting the elbow with her opposite hand and walking very cautiously. She complained of severe pains, crying several times in describing the details. Stiffness and moderate pain had been noted the previous morning. Regardless of the application of hot water bags, during the day, the pains became more severe. At times, pains radiated upward to the neck and down to the elbow. The slightest motion renewed the distress and though she had used a pillow under the shoulder for support she had had no sleep that night. Inspection of the shoulder revealed nothing. There was no swelling or evidence of inflammation. Anteroposterior motion was fairly tolerated but abduction and rotation of the extremity evoked the almost intolerable pains. There was tenderness to deep pressure to the lateral border of the acromion. The first treatment of 100 r brought no relief; the second, of 300 r produced marked benefit, while the third treatment of 400 r resulted in almost complete subsidence of the pain. No subsequent episodes of pain developed. In other cases where 400 r was applied, daily, relief was obtained after the first or second treatment.

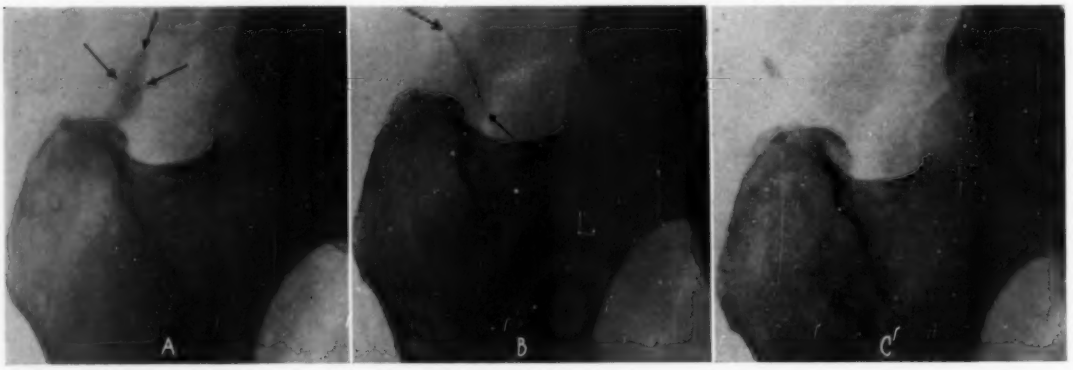

Fig. 4. Showing, *A*, calcareous deposition in the region of the tendon of the piriformis; *B*, the soft tissue density, doubtless the scar, as noted two weeks after radiation therapy; *C*, the appearance four weeks after the treatment. This patient's complaints had been regarded as a "sciatica." Physical examination revealed a negative Lasèque sign but extreme pain when abducting or rotating the thigh. There was definite tenderness to deep pressure over the greater trochanter. The first two treatments of 200 r each produced only slight benefit, but almost complete relief was reached after the third treatment of 400 r.

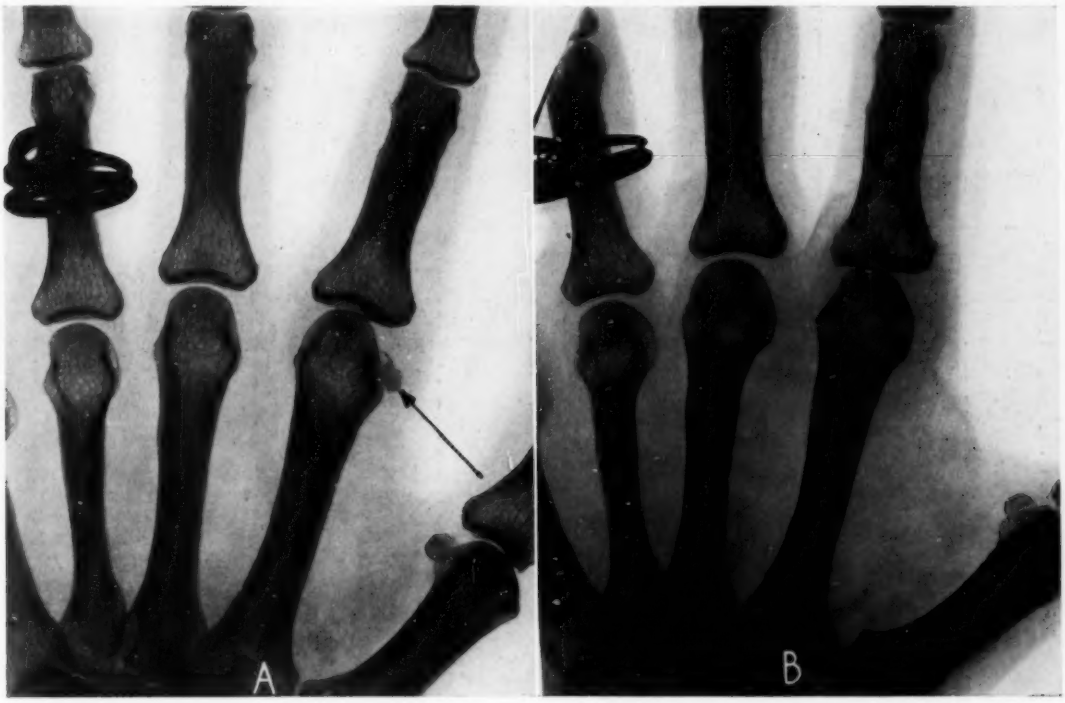

Fig. 5. Showing similar deposits regional to a metacarpophalangeal joint, *A*, and the appearance four weeks after roentgen therapy, *B*. This patient (M.M.) claimed to have "sprained" her hand repeatedly in wringing clothes. The pain became quite severe and was especially noted in attempting to flex or extend the finger. There was definite tenderness to pressure over this region. This case was treated with dosages of 600 r but these were given at intervals of several days. Relief was obtained after the second treatment.

TREATMENT

Various forms of treatment have been tried. The application of local heat is probably the oldest and most common procedure. Patients themselves often initiate the use of a hot water bag or an electric pad. An equally conservative remedy is diathermy. With it a more penetrating heat can be produced. Harris,[16] Cooperman,[10] Granger and Resnik,[15] Resnik,[25] Titus,[28] Deering,[11] Mumford and Martin,[21] and Ritvo and Resnik[26] have been ardent advocates of this method. Prolonged splinting of the involved extremity has been recommended,[6,27] either in conjunction with diathermy, massage and passive motion, or independently. In treatment of the shoulder cases, Fields[13] recommended injection of the subacromial bursa with a 5 per cent glycerin solution of iodine. Many are in favor of treating these cases surgically. It has been a common practice to remove at least a portion of the subacromial bursa. Codman[9] has pointed out that this bursa is so large that complete extirpation of it is almost impossible, and, moreover, that involvement of it is secondary in importance to the changes in the regional muscle or tendon bundles. He recommended early repair of ruptured muscle or tendon bundles and removal of deposits, if present. Kulowski[19] noted a reformation of the concretions some months after surgical removal of them from the fascial spaces regional to the knee. Carnett[6] noted the spontaneous absorption of the deposits after acute episodes of activity. Many have claimed absorption after the use of diathermy. Roentgen therapy has occasionally been mentioned.[3,12,19]

A detailed discussion of these cases would occupy too much space. The following table should suffice to present outstanding features and to compare the effectiveness of various plans of roentgen irradiation (Table 1).

TABLE I

Case	Age	Sex	Occupation	Blood Pressure	B.M.R.	Factors	Region	Involvement	Treatment	Symptoms	Flareup	Deposits
A.A.	45	F	Housewife	118/70	−22	Chilling	Shoulder, left	Suprapinatus	1/28 200r 1/30 400r 2/4 200r 2/6 200r 2/8 200r	Acute. Relief after 8 days	None	Visualized; complete absorption 6 weeks after treatment
I.H.	36	F	Housewife	126/76	−7	Dental foci	Shoulder, left	Supraspinatus	1/29 200r 1/31 450r 2/7 325r 2/9 325r 2/20 650r	Acute. Relief after 3 days	None	Visualized; complete absorption 4 weeks after treatment
							Shoulder, right	Supraspinatus	5/25 600r 5/27 600r 5/28 600r 6/1 600r	Moderate. Relief after 2 days	None	Visualized; complete absorption 4 weeks after treatment
J.Y.	29	F	Housewife	105/70		Chilling	Shoulder, left	Infraspinatus	3/29 100r 3/30 300r 4/1 400r 4/2 500r	Acute. Relief after 3 days	None	Visualized; complete absorption 4 weeks after treatment
							Shoulder, right	Supraspinatus Infraspinatus	5/21 600r 5/22 600r 5/23 600r 5/24 600r	Moderate. Relief after 2 days	None	Visualized; complete absorption 4 weeks after treatment
J.T.	39	M	Clerk	100/62		Chilling	Shoulder, left	Supraspinatus	4/3 400r 4/4 400r 4/5 400r 4/6 300r	Slight. Relief after 2 days	None	Visualized; complete absorption 4 months after treatment
R.S.	38	M	Clerk	134/96		Chilling	Shoulder, right	Infraspinatus Teres Minor	3/6 325r 3/7 325r 3/8 325r 3/9 325r	Moderate. Relief after 2 days	None	Visualized; complete absorption 4 weeks after treatment
							Shoulder, left	Infraspinatus	6/7 600r 6/8 600r	Had no symptoms in this shoulder		Visualized; no absorption after treatment

TABLE I (*Continued*)

Case	Age	Sex	Occupation	Blood Pressure	B.M.R.	Factors	Region	Involvement	Treatment	Symptoms	Flareup	Deposits
H.A.	40	F	Housewife	128/80	−4	Chronic sinusitis. Associated atrophic athritis	Shoulder, left	Supraspinatus	4/30 600r 5/2 600r 5/4 600r	Moderate. Relief in 1 day	None	Visualized; almost complete absorption after 4 weeks
R.B.	56	M	Construction foreman	112/78		Dental foci. Had associated atrophic arthritis of digits	Shoulder, right	Infraspinatus	4/6 200r 4/8 200r 4/9 400r 4/11 100r	Moderate. Relief after 3 days	Slight	Visualized; only slight amount of absorption 4 weeks after treatment
							Shoulder, left	Infraspinatus	4/8 200r 4/9 400r 4/10 400r 4/11 300r	Moderate. Relief 2 days later	None	Visualized; complete absorption 4 weeks after treatment
B.S.	45	M	Foreman of locks	112/90			Shoulder, left	Supraspinatus	5/7 600r 5/8 600r 5/9 600r 5/10 600r	Acute. Relief after 1st treatment	None	Visualized; marked absorption 4 weeks after treatment
L.V.	45	M	Superintendent of locks	98/76	−17 −15		Shoulder, right	Supraspinatus	7/11 200r 7/13 200r 7/15 300r 7/16 300r	Mild. Relief after 2 days	Twice during year	Visualized; no absorption following treatment
							Shoulder, left	Supraspinatus	7/11 200r 7/12 200r 7/13 200r 7/15 300r 7/16 300r	Mild. Relief after 2nd treatment	None	Visualized; no absorption following treatment
I.M.	36	F	Housewife	95/60	+2		Shoulder, left	Supraspinatus	9/2 300r 9/3 400r 9/5 500r	Moderate. Relief in 2 days	None	Visualized; no absorption after treatment
E.B.	34	F	Housewife	128/76	−17	Dental foci	Shoulder, left	Supraspinatus	2/17 400r 2/19 400r 2/20 400r 2/21 400r 2/24 400r 2/25 400r	Moderate. Relief in 3 days	Repeated	Visualized; no absorption after treatment

TABLE I (*Continued*)

Case	Age	Sex	Occupation	Blood Pressure	B.M.R.	Factors	Region	Involvement	Treatment	Symptoms	Flareup	Deposits
G.N.	36	F	Housewife	125/85	−16 −19		Shoulder, left	Supraspinatus	11/13 400r 11/14 400r 11/15 400r 11/16 400r 12/18 200r 12/19 200r 12/21 200r	Moderate. Relief after 3 days	Occasional but "mild"	Visualized; no absorption after treatment
D.C.	56	M	Physician	106/64	−22	Chilling	Shoulder, right	Supraspinatus	1/9 400r 1/10 400r 1/11 400r 1/12 400r 1/15 400r 1/16 400r	Acute. Relief in 5 days	Occasional but "very slight"	Visualized; almost complete absorption after 4 weeks
G.K.	55	F	Housewife	118/72	−10	Dental foci Associated atrophic arthritis	Shoulder, right	Supraspinatus Infraspinatus Triceps brachii	1/11 400r 1/14 400r 1/16 400r 1/17 400r 1/18 400r 1/20 400r 2/17 400r 2/19 400r	Acute. Relief after 5 days ..... Relief again 2 days	Acute	Visualized; almost complete absorption, 6 weeks after treatment
M.C.	37	F	Housewife	100/62	+1	Chilling	Shoulder, right	Supraspinatus Infraspinatus	1/21 400r 1/22 400r 1/23 400r 1/25 400r 1/27 400r 1/28 400r	Acute. Relief after 2nd treatment	None	Visualized; almost complete absorption 3 weeks after treatment
J.W.	55	M	Pilot on dredger	160/98	+25 +40		Shoulder, left	Supraspinatus Infraspinatus	1/21 400r 1/22 400r 1/23 400r 1/24 400r 1/25 400r 1/27 400r	Moderate. Relief after 2nd treatment	None	Visualized; almost complete absorption 6 weeks after treatment
M.B.	40	F	Dressmaker	124/86	+2		Shoulder, left	Teres minor	1/30 400r 1/31 400r 2/1 400r 2/2 400r 2/3 400r 2/5 400r	Acute. Relief after 2nd treatment	None	Visualized; almost complete absorption 6 weeks after treatment

TABLE I (*Continued*)

Case	Age	Sex	Occupation	Blood Pressure	B.M.R.	Factors	Region	Involvement	Treatment	Symptoms	Flareup	Deposits
M.S.	48	F	Housewife	116/82	−14	"Sprain 10 years ago"	Shoulder, right	Supraspinatus	3/11 400r 3/12 400r 3/13 400r 3/14 400r 3/16 400r 3/17 400r	Acute. "75% improved after first treatment	None	Visualized; complete absorption 4 weeks after treatment
T.S.	43	F	Housewife		−8	"Sprain 6 years ago"	Shoulder, right	Supraspinatus	3/26 400r 3/27 400r 3/28 400r 3/30 400r 3/31 400r 4/1 400r	Moderate; "much relief after 1st treatment"	Occasional but "slight"	Visualized; slight absorption 4 weeks after treatment
J.O.	54	M	Soldier	168/80	+2		Shoulder, right	Supraspinatus	6/12 400r 6/13 400r 6/15 400r 6/16 400r 6/17 400r 6/18 400r	Acute. "Much relief after 2nd treatment"	None	Visualized; almost complete absorption 4 weeks after treatment
G.C.	40	M	Clerk	140/100 100	+18	Dental foci	Shoulder right	Supraspinatus Infraspinatus Teres minor	6/12 400r 6/13 400r 6/15 400r 6/16 400r 6/17 400r 6/18 400r	Acute. Relieved after 2 treatments	None	Visualized; almost complete absorption 4 weeks after treatment
A.S.	49	F	Stenographer	120/85	−7	Dental foci associated atrophic arthritis	Shoulder, left	Infraspinatus	6/5 550r 6/7 550r	Had no symptoms, findings coincidental to pain in right hip		Visualized; no absorption following treatment
							Hip, right	Piriformis	3/29 200r 3/30 200r 4/1 400r 4/2 400r 4/3 100r	Acute. Relief after 3rd treatment	None	Visualized; complete absorption 2 weeks after treatments
							Hip, left	Piriformis	6/3 325r 6/4 325r 6/5 325r 6/7 325r	Had no symptoms in this region		Visualized; no absorption following treatment

TABLE I (*Continued*)

Case	Age	Sex	Occupation	Blood Pressure	B.M.R.	Factors	Region	Involvement	Treatment	Symptoms	Flareup	Deposits
R.M.	43	F	Housewife	118/60			Hip, left	Piriformis	4/15 375r 4/16 375r 4/22 375r 4/23 375r 4/25 375r	Acute. Relief after 2nd treatment	None	Visualized; almost complete absorption 4 weeks after treatment
M.M.*	44	F	Housewife	105/75	−12		Hip, right	Gluteus medius	4/5 400r 4/6 400r 4/8 400r 4/9 400r	Moderate. Relief after 2nd treatment	Repeated	Visualized; no absorption after treatment nor during year
									3/30 400r 3/31 400r 4/1 400r 4/2 400r 4/3 400r 4/4 400r	Acute. "90% relief after 1st treatment"	None	Complete absorption 4 weeks after this treatment
W.S.	50	M	Tunnel operator	110/70	−15	Chronic prostatitis. Associated atrophic arthritis	Hip, right	Obturator internus	7/3 650r 7/5 650r 7/8 325r 7/10 325r	Moderate. Relief after 2nd treatment	Followup impossible as patient left without record of whereabouts	
E.T.	43	M	Refrigerator foreman	110/76		Chronic prostatitis	Hip, right	Piriformis, obturator internus	6/11 325r 6/12 325r 6/17 325r 6/18 325r	Acute. Relief after 2nd treatment	None	Visualized; almost complete absorption 4 weeks after treatment

* A comparative analysis of the response shown by these various cases to this type of treatment indicates several axiomatic opinions: (1) that symptomatic relief can be obtained by roentgen therapy, (2) that for prolonged and likely permanent benefit, it is necessary that adequate dosage be given and that the treatment be given at a particular time—that is, during phases of acute activity, (3) that unless the calcareous deposits are absorbed subsequent flareups of activity are likely to occur and (4) that roentgen radiation definitely acts as a factor contributing to the absorption phenomenon. Note how concretely this case demonstrates such considerations. This patient had been observed the longest of any of those included in this series. Clinical and roentgenographic records established the persistence of her trouble for at least three years. The crippling episodes occurred so frequently that she finally yielded to the expectations of incapacitation at intervals of a month or six weeks. She had been hospitalized repeatedly with diagnoses of "gallbladder disease," "arthritis," "sciatica," etc. Regardless of prolonged flareups of inflammatory activity, a survey of the roentgenograms that had been taken from time to time definitely revealed the fact that no absorption of the calcareous deposits had taken place. Apparently the natural reaction processes were insufficient. Moreover, when roentgen irradiation was given during a period of only moderate symptoms the relief was transient. The calcareous deposits were not absorbed and repeated episodes of crippling pains occurred. However, with adequate administration of roentgen radiation given during the actual time of the inflammatory reaction, complete absorption of these otherwise resistant deposits resulted and no subsequent pains have occurred during a period of observation of about a year.

TABLE I (*Continued*)

Case	Age	Sex	Occupation	Blood Pressure	B.M.R.	Factors	Region	Involvement	Treatment	Symptoms	Flareup	Deposits
L.B.	46	M	Laborer on dredger	130/70	+6	Trauma; hit by log one year previously	Hip, left	Piriformis, obturator internus	11/27 330r 11/29 270r 11/30 330r 12/2 270r	Acute. Relief after 1st treatment	None	Visualized; almost complete absorption 4 weeks after treatment
B.P.	40	M	Cook	158/92		Chronic prostatitis	Hip, right	Piriformis	6/11 187r 6/12 187r 6/13 187r 6/15 187r 6/17 187r 6/19 187r 6/21 187r 6/24 187r	Symptoms had subsided before these treatments were started; no subsequent flareups		Visualized; no absorption following treatments
J.B.	41	M	Watchman	128/90		Twisted knee in falling, 10 weeks previously	Knee, left	Adductor magnus	6/15 325r 6/17 325r 6/19 300r 6/21 300r	Mild. Relief after 2nd treatment	Repeated but less severe.	Visualized; no absorption following treatment
M.M.	34	F	Housewife			Repeated "sprains" of joints of hand due to wringing of clothes		Flexor digitorum	5/20 600r 5/31 600r 6/1 600r 6/3 600r	Moderate. Relief after 2nd treatment	Occasional but "mild"	Visualized; complete absorption 4 weeks after treatment
M.J.	35	F	Secretary	98/66	+13	"Repeated stumbling"	Foot, left	Flexor hallucis	11/29 300r 11/30 200r 12/2 300r 12/3 500r 12/6 350r	Acute. Relief after 3rd treatment	Severe 10 days after this treatment	Visualized; complete absorption 4 weeks after treatment

DISCUSSION

In surveying these cases several noteworthy features stand out. Only one of the patients was under thirty; the majority were over thirty-five. There were 17 females and 14 males. Fourteen of this group were housewives. The duties of a housewife, here in the tropics, are not usually very strenuous. Undue muscle strain can hardly be associated with the occupation of many of the others, though 6 of these patients attributed their trouble to some remote injury—in most cases, an injury which might ordinarily be considered trivial. The pilot on the dredger and the tunnel operator probably endured the greatest physical activity; the refrigerator foreman, both physical exertion and extreme contrasts in temperature. All types of physique were represented, some very slender and others overly stout; 2 weighed less than 100 pounds and 3 weighed over 200 pounds. Relatively low blood pressures were the rule, only 5 of these patients showing pressures commensurate with their age. Basal metabolic tests were not possible in all cases, but among the 21 patients tested there were only 3 abnormal increases, and only 8 plus values—the rest showing lowered rates which appeared to be significant. Exclusive of gastrointestinal conditions which might have been concerned with toxin absorptions, there were conspicuous foci of infection in 10 of the cases. These were casual findings as exhaustive surveys were seldom possible.

The variety of localization of the calcareous deposits was a finding especially to be emphasized. This study has convinced us that each case of this sort must be studied individually. The changes, in any particular region, are not invariably found in any one tendon, muscle bundle or fascial space. One shoulder case may show involvement in the region of the supraspinatus; another, about the infraspinatus and still another, about the teres minor or even the triceps brachii. One or more of these muscle bundles or tendons may be intimately concerned. In like manner, as far as the hip is concerned, changes may be noted about the tendon of the gluteus medius, or the piriformis, or the obturator internus. The knee and small joints show similar possibilities. These localizations can best by studied by stereoscopic projections but, as shown in Figure 1, much can be visualized in the flat film.

For the hip lesions, stereoscopic projections are even more important. Figure 2 demonstrates the apparent similarity of relations of the deposits, as seen on the flat film, even though they may concern quite widely separated tissues.

An accurate localization of these changes is very important. Certainly this would be true for cases to be treated surgically. It is just as important for those to be treated by roentgen irradiation. A clear concept of the actual site of the pathology is necessary in order to properly direct the rays so as to deliver the necessary large dosage through the smallest portal possible.

Another feature to be emphasized, in these cases, concerns the response to roentgen therapy. The results as seen clinically and by roentgenographic follow-up seem to fall into three groups. In the first group we might consider those cases which had had no clinical complaints but in which calcareous deposits had accidentally been found. These cases, followed for over a year, continued to be symptom-free but the roentgen therapy failed to produce absorption of the deposits. In the second group, we might consider those cases in which the symptoms were mild or moderate but which showed definite deposits before the treatment. For these patients there was marked alleviation of symptoms or complete control of them and the deposits were either partially or completely absorbed. Some of these patients did have subsequent episodes of pain but most of the group volunteered the remarks that the pains were never as severe as before the treatments. The most spectacular results were obtained among the third

group—those treated during episodes of very acute pain. A single treatment frequently changed these patients from the status of a suffering cripple to that of an enthusiastic patient. Some remarked about a "tingling" or a "drawing" sensation in the aching region, during the course of the peutic measures are helpful but most regimens of that nature require days and even weeks of inactivity, and often hospitalization. Surgery might be used to hasten relief but even with it there follows a relatively prolonged period for convalescence and graduated exercises. The

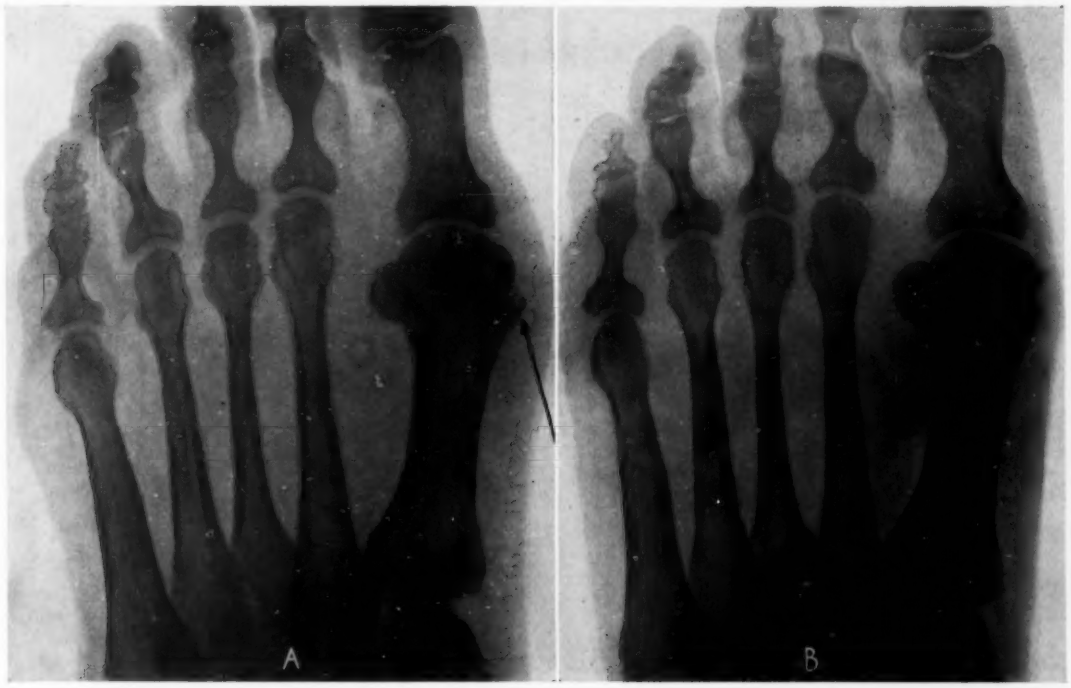

Fig. 6. Showing, *A*, deposits regional to a metatarsophalangeal joint and, *B*, disappearance of the concretions four weeks after roentgen therapy. This patient (M.J.) had been limping for several days because of swelling and pain about this joint. There was no definite evidence of inflammation in this region. Roentgen therapy was given in the dosages listed in Table 1. Relief of symptoms was not as spectacular in this case, probably because of continued use of the foot, but after the second week no flareups of activity occurred.

first treatment, and a striking palliation of the pains within a few hours. A number of these patients were brought to the clinic on a stretcher, for their first treatment; in a wheelchair, for the second, and they were able to walk in, for the third. All of the cases which were treated during such acute stages showed rapid absorption of the calcareous deposits with no subsequent flareup of the pain.

If untreated, these cases go on suffering for days and often for weeks. Heat, splinting and analgesics are sometimes only partially palliative. Various physiotherapy course with roentgen therapy is quite different. If properly given, this type of treatment produces almost immediate relief of pain; disability is reduced to only a few days and hospitalization is practically unnecessary.

The physiological processes concerned with the absorption of the deposits remain problematical. Carnett[6] has noted that deposits sometimes disappear without any treatment and merely on the basis of an acute episode of activity. A number of the cases reported here had had repeated acute attacks of crippling pains without

FIG. 7. This case is included to show the similarity of findings in the condition which is sometimes called "Pellegrini-Stieda's disease." There had been the usual background of trauma, a twist of the knee, about ten weeks previously. Roentgenogram studied about one week after the injury was reported negative and the patient had been kept on duty until his complaints became so severe that he was sent into the hospital. At the time roentgen therapy was applied the symptoms were only moderate. Though these abated, apparently in response to the treatment, the deposits were not absorbed. This treatment was given early in the course of these studies. The response to the regimen ultimately adopted as applied to similar lesions in other locations suggests that if this case had been treated during phases of acute reaction with daily applications of 400 r up to a total of about 2,400 r (using multiple portals), more spectacular results might have been obtained.

FIG. 8. Calcareous para-arthritis of the elbow. Note the mottled densities regional to the lateral condyle of the humerus; the similarity in appearance, here, with that in so-called "Pellegrini-Stieda's disease," about the knee. There was no background of trauma in this case; simply the complaint of stiffness about the joint and a dull pain. This patient was a housewife, aged forty-seven, of the higher social stratum, having no significant occupational strain. A calcareous deposit was also found in her shoulder, regional to the tendon of the supraspinatus. There was no tenderness concerned with the latter and no impairment of motion. There was definite tenderness to pressure about the lateral aspect of the elbow. A search for foci of infection revealed a dental abscess. This case was not treated by roentgen therapy for it was believed that too little inflammatory reaction existed at the time of her coming to the clinic; her symptoms were too mild. For that reason she was given diathermy. The condition was described to her and she was advised to return for another form of treatment (roentgen therapy) in case of another flareup with greater severity of pain. The diathermy produced benefit but later recheck of the elbow revealed the fact that the deposits had not been absorbed. This reproduction is included to present a case of "para-arthritis," concerned with the elbow; as shown, this condition might be found regional to any of the joints of the extremities. It is also intended to illustrate a case where roentgen therapy was delayed until a time when more permanent benefit can be expected.

any absorption of the deposits. Moreover, in some of the cases where there had been only mild or moderate symptoms, absorption occurred after roentgen therapy. These considerations lead us to believe that as a result of the roentgen irradiation there had been set up some degree of inflammatory reaction comparable to that which Nature stirs up during episodes of acute symptomatology. At any rate, it appears that the roentgen irradiation contributes to the absorption potential and while doing so it camouflages the entire process by a most effective relief of the pain which Nature otherwise seems to re-

quire. However, it must be repeated that the irradiation by itself does not seem to be effective. Findings of calcareous deposits without associated symptoms do not warrant the treatment. It may even be well to temporize with cases presenting only mild symptoms so that the tissues are spared for an occasion when with more severe symptoms the irradiation can be thoroughly effective. However, these patients must not be lost; they should be advised as to the opportune time for treatment.

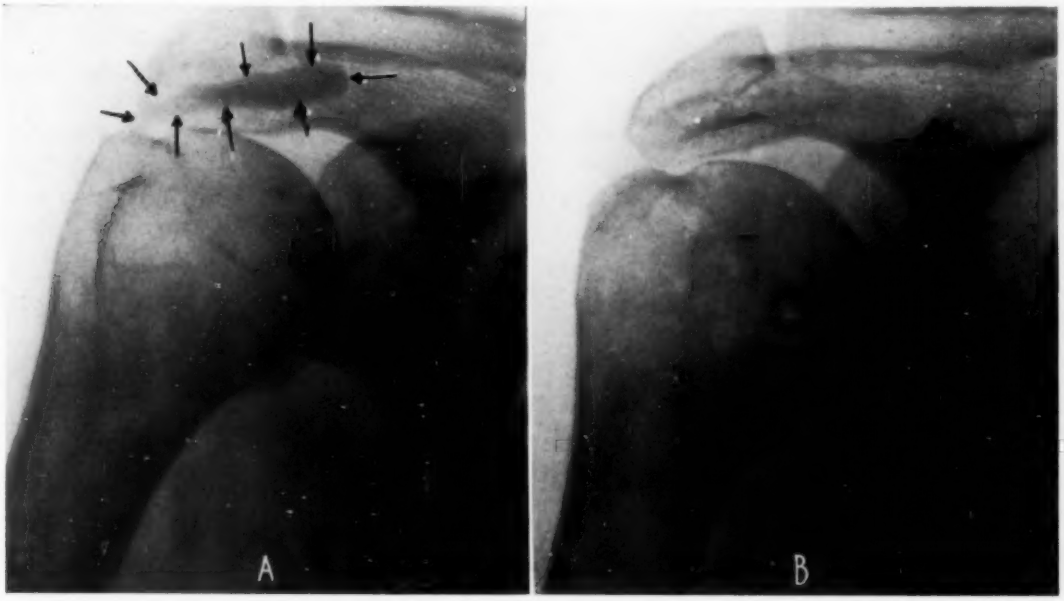

Fig. 9. Large dense calcification concerned with the tendon of the supraspinatus. A synopsis of this case is included in Table 1, patient T.S. This reproduction is added to show that even these large deposits can be absorbed, when treated at the proper time, i.e., during a stage of acute activity; this case also shows that the absorption may be a slow process for here only slight change was noted when rechecked one month after treatment, but as shown in *B*, there remained only a slight mottling of calcific density, three months after the treatment. This patient has been seen at intervals for over a year; she has had no recurrence of acute pain and even the minimal stiffness and pain (which continued during the first month after treatment) have entirely disappeared. Previous to roentgen therapy she had been having episodes of crippling pains, at intervals, for about six years. Apparently, the inflammatory reactions concerned with these, per se, were insufficient to effect absorption of the mechanical excitants of irritation—the calcareous deposits.

It can be noted in the table that the most effective regimen of treatment consisted of daily administrations of 400 r, giving up to a total of 2,400 r (this dosage, as measured in air without the consideration of back-scattering). The skin should be spared* as much as possible by the use of multiple portals. In the case of ball and socket joints, such as the shoulder or the hip, this can be accomplished without any appreciable change in the tissue depth by maintaining the same position, as far as the patient is concerned, on the table, but placing the extremity first in internal rotation and later in external rotation, thereby covering the region to be treated with two different skin areas. The size of the portals was varied according to the depth of the pathological focus and the certainty of adequately covering it with the radiation. Portals as small as 2 or 3

* All patients should be instructed to apply Dodd's solution to the irradiated area, twice daily, for a period of at least one month after the completion of the series. Special warning must be given to patients receiving treatment to the hip. For two reasons a very severe dermatitis can be expected here: (1) the portal is relatively large and (2) the region is early subjected to trauma imposed by sitting and to greater amounts of sweat.

cm. in diameter were used in the cases of the smaller joints; for the shoulder cases, a 3.5 by 7 cm. portal was used—the longer dimension being aligned over the particular muscle tendon which was found, roentgenographically, to be involved. In the hip cases, the first treatment was usually given through a 9.5 by 12 cm. portal, but thereafter the portal was reduced to 7.5 by 9.5 cm. Anatomical landmarks were used to guide the positioning of these portals but it became a regular practice to check the accuracy of the field by having the patient palpate the area and with one finger locate the site of greatest tenderness. This measure insured the correctness of the field and permitted reduction in its size.

The quality of the rays varied according to the thickness of interposing tissues. The lowest kilovoltage used was 137, as applied to the smaller joints; most of the shoulder cases were treated with 140 kv. technique, while the hip cases received 200 kv. therapy. The lightest filtration was the equivalence of 5 mm. of aluminum; for the shoulder cases either this or 0.25 mm. copper plus 1 mm. aluminum was used, while 0.5 mm. copper plus 1.0 mm. aluminum was used for treatment of the hip cases.*

Due consideration was given to the type of concretion. Some of these cases showed a very dense, sharply outlined deposit as visualized roentgenographically. It is probable that in these the concretion was of the type which Brickner[4] found to be composed of calcium oxalate and carbonate. These appeared to be more resistant to absorption but complete absorption did take place even with this type. Other cases showed more mottled and less sharply outlined densities which appeared to represent substance of considerably greater radiotransparency than bone. These were probably made up of amorphous calcareous débris. Absorption of this type of material occurred much quicker.

Figures 2, 3, 4, 5, 6, 7, 8 and 9 are included to illustrate the variety of these cases and the response to this type of treatment.

This presentation has been limited to those cases in which the diagnosis appeared to be amply established both clinically and roentgenographically. Cases presenting clinical evidence of this condition, but lacking the roentgenographic evidence of the calcareous deposits were, as a general rule, treated with diathermy. However roentgen therapy was applied in the more obstinate cases of this type, those failing to respond within a week or so, and it was found that doses of 400 r, applied daily, were strikingly effective. In these cases, the total dosage was seldom carried above 1,600 r (as measured in air).

It must be re-emphasized that the summation of these treatments represents a relatively large total dosage of roentgen radiation. Moreover, this large dosage is given within a very short period of time. It is very important, therefore, that multiple portals be used and that the dimensions of the portals be reduced to the minimum.

CONCLUSIONS

1. In cases manifesting aches or "neuralgic pains," which are concerned with the motion of a joint in the extremities, one should consider the possibility of a localized inflammatory condition more or less limited to one or several muscle tendons included within a sector of the joint periphery—a "para-arthritis."

2. Such cases should be analyzed in terms of the particular muscle bundles involved.

3. Roentgen therapy, if properly directed and given in adequate dosage, very quickly effects subsidence of symptoms. The mere findings of calcereous deposits

* Most of the cases included in this report were treated with a G. E. model KX-3, valve tube half wave rectification; in the case of the 140 kv. (peak) technique, with filtration of 5 mm. Al, the half-value layer was 0.3, having an effective wave length of 0.205 Å; with the same kilovoltage and filtration of 0.25 mm. Cu plus 1.0 mm. Al, the half-value layer was 0.53, having an effective wave length of 0.182 Å; when 0.5 mm. Cu plus 1.0 mm. Al was used, with 200 kv. (peak) the half-value layer was 1.12, having an effective wave length of 0.145 Å.

are insufficient grounds for this type of treatment. The response to roentgen irradiation, as evidenced by clinical and roentgenographic follow-ups, is effective in proportion to the degree of the symptomatology, or in other words, probably to the degree of inflammatory reaction. With proper selection of the cases as to the most optimum time for this type of treatment, even the most dense calcareous deposits can be absorbed.*

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HYPOPROTEINEMIA AS A FACTOR IN THE RETARDATION OF GASTRIC EMPTYING AFTER OPERATIONS OF THE BILLROTH I OR II TYPES*

By R. P. BARDEN,† I. S. RAVDIN *and* W. D. FRAZIER
PHILADELPHIA, PENNSYLVANIA

THE roentgenologist is frequently requested by the surgeon to study a patient who a short time previously has had an operation for gastric or duodenal ulcer with restoration of gastrointestinal continuity but whose stoma is not functioning properly. Such a condition has been observed when the restoration of gastrointestinal continuity has been made by either the Billroth I or Billroth II procedures. Kirklin,[2] and Ravdin, Pendergrass, Johnston and Hodes[4] have shown that even under favorable operative conditions the new stoma may not function normally, as determined by roentgenoscopic observation, for some time following operation. These authors have warned against the too rapid acceptance of the roentgenoscopic observation of gastric retention as evidence that a mechanical defect in the anastomosis is responsible for the malfunction of a newly formed stoma. The frequency with which we have observed such malfunctioning stomata later to function normally, provided the patient can be carried through the crisis, is excellent evidence that obstruction due to an improper anastomosis is rare and that other factors, as yet not generally recognized, may be playing an important part in the impediment to gastric emptying.

It has been generally agreed that in all instances of anastomosis there occurs in the area of the stoma a variable amount of edema, the result of trauma. Such edema, which is temporary, may for a short time delay the gastric emptying. The interference with nervous innervation, especially where a resection has been done, may also be a factor in the process.

Recently Mecray, Barden and Ravdin[3] have demonstrated that factors other than the simple edema of trauma, or a technical arrangement of the anastomosis, or interference with innervation are frequently the underlying basis for the failure of the stomach to empty. The edema of trauma will not persist for days. If, however, as a result of prolonged protein restriction, the patient comes to operation in a state of hypoproteinemia, the most important mechanism for holding the circulating fluids in the blood vessels becomes disturbed and edema may result.

Even if edema is not manifest at operation, the administration of large amounts of fluid, especially saline solution, in the postoperative period may precipitate an edema. Furthermore, a protein concentration of the serum at a level where latent edema is present will intensify the manifest edema associated with trauma and will prolong the fluid retention in the tissues following trauma.

The high mortality which is so often associated with a secondary operation after the Billroth I or II procedures makes it necessary that we understand the underlying pathologic physiology of the primary condition if these desperately ill patients are to be spared a second laparotomy with its attendant risk.

In this paper we wish to report observations on the effect of a hypoproteinemic state on the gastric emptying time in the

* From the Department of Roentgenology, the Harrison Department of Surgical Research, and the Department of Surgery, School of Medicine, University of Pennsylvania, Philadelphia.

† Part II of thesis submitted to the Faculty of the Graduate School of Medicine of the University of Pennsylvania in partial fulfilment of the requirements for the degree of Doctor of Medical Science (D.Sc. (Med.)) for graduate work in radiology.

dog and man following various gastric operations.

EXPERIMENTAL DATA

Dogs were chosen as the experimental animal for the reasons given in our earlier paper.[3]

Hypoproteinemia was induced by diet and plasmapheresis. The protein content of the diet was approximately 1 per cent, and the vitamin requirements were adequately controlled. Each animal received double its caloric requirements daily. The gastric emptying time and serum proteins were determined at least weekly.

One group of dogs was made hypoproteinemic and then subjected to pyloric resection with restoration of the gastrointestinal continuity by the Billroth I or the Billroth II principle. The gastric emptying time was determined at critical periods of the experiment. A second group of dogs which had had operations of the Polya type performed at least a year previously was also studied.

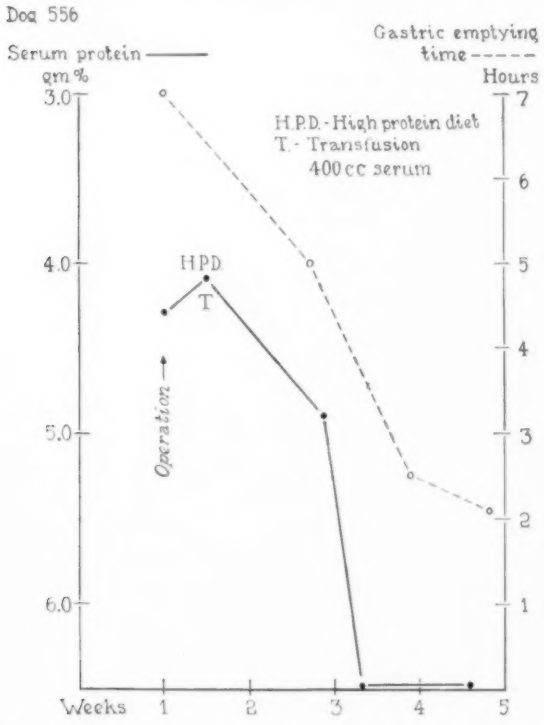

FIG. 1. Dog from Group I. Serum protein and gastric emptying time in Dog No. 556 subsequent to a Polya operation.

FIG. 2. Roentgenoscopic examination in a dog with low serum protein. Active gastric contractions are present.

In Group I, the dogs were operated on while the serum proteins were low. There occurred a definite delay in the gastric emptying despite strong gastric contractions visible by roentgenoscopic examination (Figs. 1 and 2). All of the animals showed speeding up of the gastric emptying time as the proteins were restored to normal.

When fluids were withheld in one of these dogs for thirty-six hours, the gastric emptying time was speeded up as dehydration resulted in an elevation of the serum protein level. Following this, the administration of normal saline solution intravenously resulted in a fall in the serum proteins and a retardation of the gastric emptying time (Fig. 3).

In Group II, which consisted of dogs which had been subjected to a Polya operation many months before the beginning of this experiment, the gastric emptying time was studied repeatedly while the dogs were on a normal animal

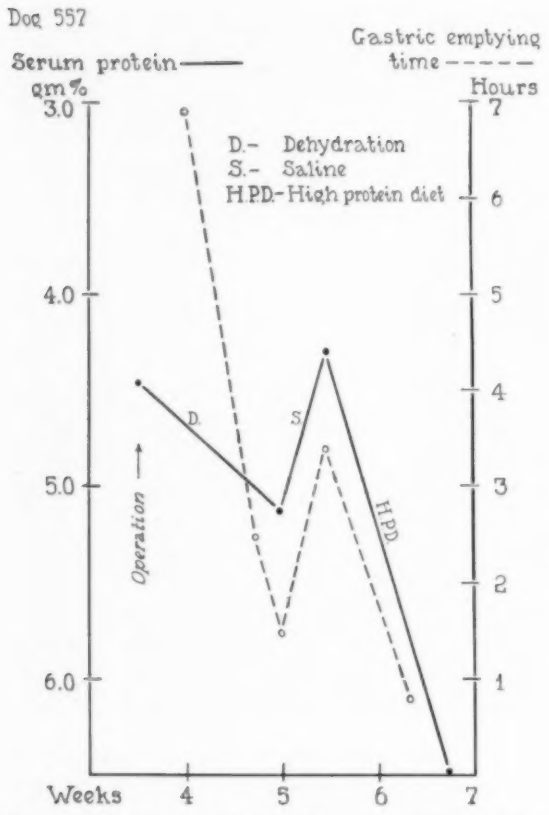

FIG. 3. Effect of dehydration, hydration and a high protein diet on the gastric emptying time in a hypoproteinemic dog subsequent to a Polya operation.

house diet and after varying periods of a low protein diet and repeated plasmapheresis (Fig. 4).

The dogs in this group showed a marked retardation of the gastric emptying time as the serum proteins fell, demonstrating that hypoproteinemia could cause retardation through a stoma which under normal conditions of nutrition functioned perfectly.

CLINICAL OBSERVATIONS

It is of importance to determine whether the conditions which were imposed on the dog and which resulted in a marked retardation of gastric emptying time occur in man. Jones and Eaton[1] and Ravdin and Rhoads[5] have published evidence which would indicate that an analogous state is observed in man more frequently than is generally recognized.

The following case reports are examples of the clinical occurrence of this train of events.

CASE 1. C. P., male, aged fifty-four, was admitted to the surgical service of Dr. I. S. Ravdin in July, 1936. The patient had had ulcer symptoms for fifteen years, but during the six months prior to admission, pain had become more severe, even on a restricted diet, and nausea and vomiting occurred at very frequent intervals. He had lost 30 pounds in weight. Gastrointestinal roentgen examination disclosed a duodenal ulcer with pyloric obstruction. Total serum protein was 5.7 grams per cent. Because of the low level of the serum protein he was given several transfusions before operation. A posterior gastrojejunostomy was then performed. During the first seven days after operation his serum protein level fell to 4.9 grams per cent despite three transfusions. Large quantities of fluid were recovered by drainage during this period. This was balanced by the administration of equal amounts of

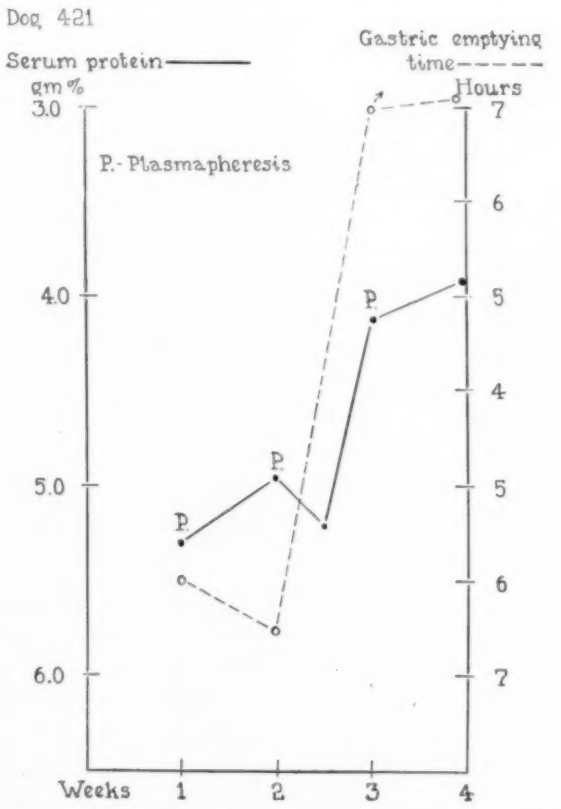

FIG. 4. Serum protein concentrations and gastric emptying time in Dog No. 421. Polya operation performed one year previously.

fluids by intravenous infusion, largely in the form of 5 per cent glucose in normal saline solution. His fluid intake was then sharply reduced, transfusions were repeated, and he was given vigorous protein therapy. There followed a rise in his serum protein level first to 5.9, then to 6.1 grams per cent and the amount of fluid retention in the stomach dropped precipitously. The remainder of his convalescence was uneventful. At the end of two months he had gained 20 pounds, the serum protein was normal and roentgen examination revealed a normally functioning stoma. Figure 5 shows the relation of serum protein to fluid output from his stomach.

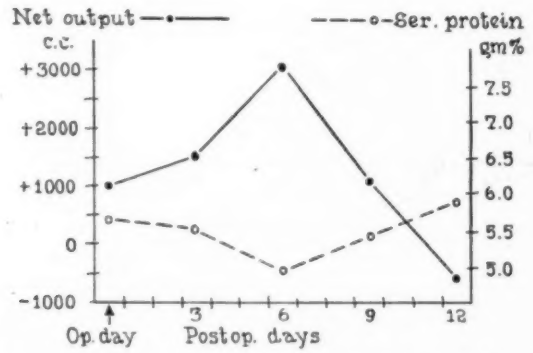

Fig. 5. Comparison of output by siphon drainage from the stomach and serum protein concentration.

Case II. T. A., male, aged twenty-three, was admitted to the Hospital of the University of Pennsylvania on the service of Dr. I. S. Ravdin in January, 1935. During the year prior to admission he had had increasingly frequent attacks of severe epigastric pain following eating. He therefore restricted his diet. Two days before admission he had several bloody stools associated with marked weakness and vertigo. Examination revealed marked pallor and epigastric tenderness. His hemoglobin was 22 per cent. Following four transfusions the hemoglobin was 68 per cent. Roentgen examination of the gastrointestinal tract disclosed a penetrating duodenal ulcer. A Polya operation was done. After operation his progress was satisfactory except for persistent evidence of obstruction at the stoma. For twelve days large amounts of fluid were obtained by suction drainage. At this time repeated transfusions and a reduction of his fluid intake resulted in marked improvement (Fig. 6). Vomiting ceased

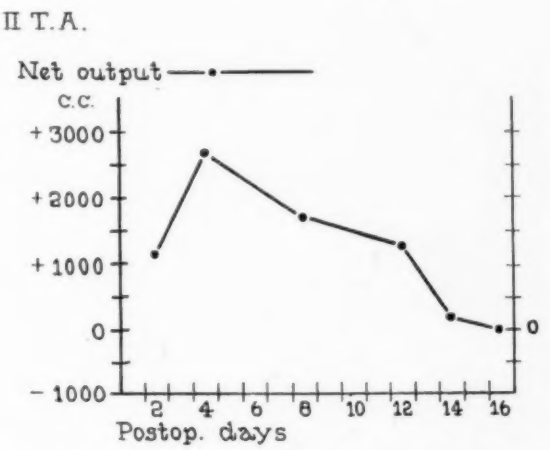

Fig. 6. The amount of fluid obtained by siphon drainage from the stomach of a patient after a Polya operation.

and the remainder of his convalescence was uneventful. Roentgen examination on his thirteenth postoperative day revealed a dilated stomach, which emptied through the stoma very slowly, and contained a large residue even after eighteen hours (Fig. 7). One month after operation his stomach emptied in three hours (Fig. 8). The clinical course and roentgen find-

Fig. 7. Case II. Thirteenth postoperative day. Polya operation. Roentgenogram showing stomach eighteen hours after barium meal.

FIG. 8. Case II. Thirty-sixth postoperative day. Polya operation. Roentgenogram showing stomach three hours after barium meal.

ings are sufficient evidence that the temporary obstruction at the stoma was due to the mechanism which we have described.

CASE III. H. D., male, aged thirty-four, admitted to the surgical service of Dr. I. S. Ravdin, in October, 1934. His history was characterized by increasingly frequent attacks of nausea, vomiting, and abdominal pain, weakness, and loss of weight during the year prior to admission. Physical examination revealed emaciation, marked dilatation of the stomach and a hard mass in the right epigastrium. His hemoglobin was 22 per cent, which was raised to 50 per cent by transfusions. A posterior gastrojejunostomy was then performed, short circuiting around a large fixed mass at the pylorus. In spite of daily transfusions this patient's serum protein level was 4.9 grams per cent six days after operation. During this time he poured out large amounts by suction drainage and received large amounts of parenteral fluids. There was marked pitting edema of the extremities. When the amount of intravenous saline was greatly reduced and transfusions continued daily, the serum protein rose to 6.3 grams per cent. The output from his stomach then fell abruptly, as shown in Figure 9, and the patient showed definite clinical improvement.

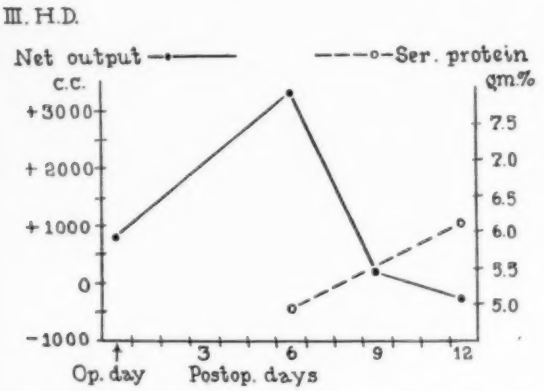

FIG. 9. Fluid output by siphon drainage from the stomach and serum protein level after a posterior gastroenterostomy.

DISCUSSION

That the general state of the patient may be gravely disordered by improper diet was recognized by Burton in 1621. In his "Anatomy of Melancholy," he quotes Fernelius as stating that "diet is the mother of diseases." The interference with a normal diet, which many of the patients coming to operation for gastric and duodenal ulcer, or gastric cancer, present, may have been a very real one. Many of these patients have had a prolonged, self-imposed, protein restriction. Others, because of gastric or duodenal stenosis with recurrent vomiting, suffer serious nutritional deficits. The hypoproteinemia which these patients may manifest is therefore due to a combination of circumstances. Furthermore, while in the experimental animal a diet can be supplied which is not unbalanced except for protein, in man the problem is frequently much more complicated, for in man there may be an associated vitamin deficiency. And since certain of the vitamins, especially B_1, affect gastrointestinal motility, the delay in gastric emptying in certain of these patients may be due to a combination of factors.

Whether a vitamin B_1 deficiency which has not progressed to an advanced stage will seriously affect gastrointestinal mo-

tility may as yet be questioned. That the protein deficiency alone is capable of producing a retardation of gastric emptying time in the dog we believe we have demonstrated, for in these animals a potent vitamin B concentrate (Harris) was given in amounts sufficient to prevent a vitamin B deficiency. Moreover, while a vitamin B_1 deficiency produces intestinal atony, the stomachs of our dogs have shown active peristaltic activity.

There are several possible explanations for the observed delay in gastric emptying time in hypoproteinemic patients and animals: first, the reduced vitality observed in the hypoproteinemic dogs may be expressed in a diminution of gastric activity; second, the edema of the gastric tissues may interfere with effective muscle contraction and, third, the reduction in the size of the stoma, coincident with the edema, may so interfere with emptying as to result in the observed retention. We are inclined to believe that this latter explanation is the correct one, providing a vitamin B deficiency does not exist.

All of the animals with total serum proteins of 4.0 per cent or lower showed gross edema of the stomach at post mortem or operation. The same state has been observed in human patients with hypoproteinemia. When operation has been resorted to, the increased edema incident to trauma further reduces the caliber of the stoma.

Sections of the specimens removed from the stomach demonstrate the edema (Figs. 10 and 11). We have examined the stoma at post mortem in a number of hypoproteinemic dogs subjected to the Polya operation, in whom the period following operation was sufficiently long to permit of subsidence of the reaction to the trauma of operation. Nearly uniformly the edema was such as to cause a very marked reduction in the size of the stoma.

It was a general observation during roentgenoscopic examination of the animals having edema, that the gastric tone was normal or increased, and that the peristaltic waves were equal to, or greater than, their normal depth. The roentgenoscopic picture was similar to that observed during pyloric obstruction. There was not the slightest evidence of atony.

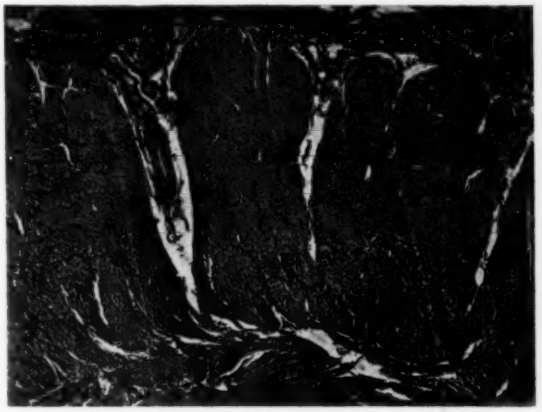

Fig. 10. Photomicrograph showing submucosa and muscularis of the stomach of a normal dog. Total serum protein 6.20 grams per cent (×50).

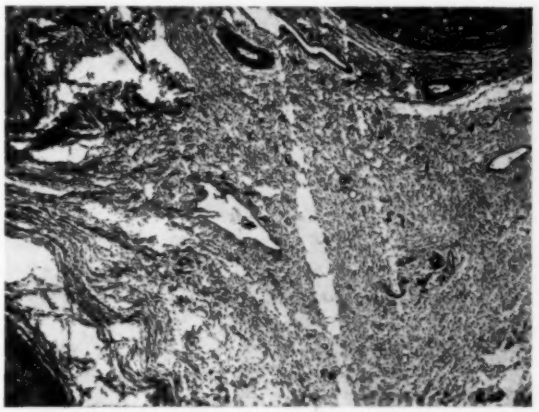

Fig. 11. Photomicrograph showing edema of the submucosa of an animal having total serum protein of 2.73 grams per cent (×50).

Clinically, latent or manifest edema is most frequently seen in cases of nitrogen starvation, general malnutrition, purulent, and serous drainage, hemorrhage, severe diarrhea, and following the administration of large amounts of sodium salts. There is good evidence that as the plasma proteins are reduced from their normal levels, diminishing amounts of fluid and sodium salts are required to cause edema. It must be remembered that the clinical edema of the

subcutaneous tissues is but an external manifestation of a general process and, as such, requires active therapy if the patient is to survive. The therapeutic aspects of this lesion we plan to discuss in a subsequent paper.

At the present time, another group of experiments is in progress. We are studying the motility and pattern of the small intestine of the dog under the same conditions that prevailed in the study of gastric emptying time. Our studies are not complete, but several facts stand out. The results of the experiments on gastric emptying have been confirmed. In animals with hypoproteinemia, there is very definite retardation of the barium in its passage through the small intestine, though this slowing is not of the same degree as the delay in gastric emptying. The retardation in the small intestine is not due simply to the delayed gastric emptying time, but to a disturbance of the small intestinal physiology. This is distinctly shown by the marked alteration in the intestinal pattern, as compared with that of a dog with a normal level of the serum protein.

SUMMARY

Data have been presented on the effect of a reduction of the serum proteins on the gastric emptying time in the dog and man after operations of the Billroth I or II type. In general, the gastric emptying time increases as the serum proteins decrease in concentration. The increase in gastric emptying time, associated with edema of the gastric wall, is accompanied by a decrease in the serum protein and in our experiments was not related to a vitamin deficiency. Studies which we are now conducting indicate that the small intestines are affected independently, and by the same mechanism. The roentgenologist must be cautious in diagnosing gastric retention after operations of the type described as an evidence of a mechanical defect of the anastomosis.

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THE EFFECTS OF IRRADIATION ON GLIOMAS*

By C. H. FRAZIER, M.D., Sc.D., BERNARD J. ALPERS, M.D., E. P. PENDERGRASS, M.D., *and* GEORGE W. CHAMBERLIN, M.D.

PHILADELPHIA, PENNSYLVANIA

INTRODUCTION

ANY investigation of the irradiation of gliomas must be concerned primarily with two problems: (1) What are the effects of irradiation on the various types of gliomas as seen in histological studies? (2) What are the possibilities in radiation therapy as an adjunct to surgery? The first question has been answered in part by the studies of previous investigators (Bailey, Sosman and Van Dessel,[2] Alpers and Pancoast,[1] Olivecrona and Lysholm[5] and Bremer, Coppez and Sluys.[3]) These indicate that histological changes may be detected following irradiation of the medulloblastomas particularly, and to a lesser degree of the tumors of the glioblastoma multiforme and the astrocytoma groups. Irradiation has not been able to cure any of the many types of glioma, but it has exerted some influence on the tumors mentioned, particularly on the medulloblastomas. Minor changes have been recorded after irradiation of the other types of glioma but they are neither sufficiently universal nor pronounced to be of much importance. Histological studies have demonstrated, therefore, that the irradiation of gliomas is followed by changes in the structure of these tumors attributable to the irradiation. The results have fallen far short of a cure, however, even in the most susceptible of the tumors. The problem then resolves itself into a consideration of whether irradiation has sufficiently good possibilities as a means of treatment to justify its continued use, whether it has been valuable in prolonging life where surgery has failed, and whether with the more intensive forms of treatment which are in use today we may look forward to even more help from irradiation than we have received in the past.

MATERIALS AND METHODS

Thirty cases of glioma were selected for study. While many more were available, only in these 30 were histological specimens available before and after irradiation. It was decided that only in instances where pre- and post-irradiation specimens were available was it possible to reach a conclusion concerning the efficacy of irradiation. The types of glioma were distributed as follows:

TABLE I

TYPE AND NUMBER OF GLIOMAS IRRADIATED

Medulloblastoma	12
Glioblastoma multiforme	7
Astrocytoma	6
Ependymoma	2
Oligodendroglioma	3
Total	30

It is apparent from this table that not all the various types of glioma were subjected to irradiation but those treated represent the more common types of tumor of this group.

DISCUSSION OF IRRADIATION FACTORS

The analysis of all irradiation data should be made on the basis of three fundamental factors, namely, the quantity of radiation, the quality of radiation, and the time factor.

The quantity of radiation is best expressed for the purpose of this paper as total tumor dose in roentgens. In order to analyze the cases presented in this series, it became necessary to divide them into three groups as follows:

TABLE II

Group	Classification	Tumor Dose
1	Inadequate treatment	Less than 1,000 r
2	Moderately treated	1,000–2,000 r
3	Adequately treated	More than 2,000 r

* From the Departments of Neurosurgery and Radiology of the Hospital of the University of Pennsylvania, Philadelphia. Read at the Thirty-seventh Annual Meeting, American Roentgen Ray Society, Cleveland, Ohio, Sept. 29–Oct. 2, 1936.

This classification has been adhered to in all of the different types of glioma presented. The tumor dose in roentgens is purely arbitrary. Possibly the figures for cases classified as adequately or moderately treated may be entirely too low. This we hope to decide from the histological data. Obviously, a tumor dose considered adequate for the medulloblastoma group is probably inadequate for the more resistant glioma types, but for the purpose of determining the relative effect of roentgen therapy it was advisable to use the above standards.

In the following irradiation data it will be noted that some of our cases were treated with 200 kv. at 4 ma. current. The equipment at this time was supplied with a mechanical rectifier so that the 200 kv. designates peak voltage. Since 1932 our cases have received treatment at 165 kv. constant potential at 15 ma. current. This equipment is composed of a single LeTour circuit, the ripplage at 15 ma. being approximately 8 per cent.

For those cases treated before the introduction of the standard roentgen, we have taken 300 ma-min. as an erythema equivalent to 800 r measured in air.

The target skin distance has, in all cases, been 50 cm.

Measurements of the scattered radiation are based upon an 8×16 cm. field, and the figures are in accord with those obtained by other observers. For a field of this size we have used 29 per cent scattering. The total number of r delivered in air to each portal was added and from this the scattering was determined for that particular portal. In our computations we have not considered the quantity of exit radiation.

The depth dose percentage has been obtained from the tables presented by Weatherwax.[8]

The half-value layer for 0.5 mm. Cu and 2 Al is 0.88 mm. Cu, the effective wave length being 0.17Å. For Thoraeus filter equivalent to 2 mm. Cu, the half-value layer is 1.75 mm. Cu and λ effective 0.125Å. These figures are accurate for the present system of therapy with 165 kv. constant potential. We have used the same effective wave length for those cases which were treated at 200 kv. (peak) pulsating. This probably introduces a small factor of error.

The time factor must include a consideration of the daily dosage, the interval between doses, the duration of the series and the interval between series. So little is known as yet concerning the biological effect of roentgen rays that it is impossible to discuss the effect of time in relation to tissue recovery. It is known, however, that the effects of irradiation are not entirely and completely cumulative, but that there is a certain rate of loss of radiation from the tissues. The loss may be as high as 60 per cent during the first twenty-four hours following a first exposure, and we have reason to believe that almost all radiation activity is lost at the end of six weeks following a series. Certainly a patient treated with 2,000 r delivered in one month should not be presented in the same group as a patient who receives a total dose of 2,000 r delivered in ten months. Although it was found necessary to consider total tumor dose, regardless of the time interval, for the general classification, we have attempted to analyze this factor in the subsequent discussion.

The average daily dose delivered was approximately 120–150 r (measured in air). In general, treatment was started with a single administration of 50 r. This was gradually increased by 25 r per day. If the patient showed no constitutional reaction or evidence of increased intracranial pressure, the daily treatment was increased to 200 r. In a few patients it was necessary to deliver less (100 to 150 r), sometimes dividing the daily dose into one morning and one mid-afternoon component.

The r per minute output with 0.5 mm. Cu was approximately 40; with 2.0 mm. Cu or equivalent the intensity averaged 15 r per minute.

MEDULLOBLASTOMAS

The histological response of the medulloblastomas to irradiation varied rather widely as will be seen from the following table:

Table III

RESPONSE OF MEDULLOBLASTOMAS TO IRRADIATION

Case	Degree of Response	Irradiation
H. D.	+++	Adequately treated
W. P.	+++	Moderately treated
J. M.	++	Adequately treated
P. H.	++	Adequately treated
J. L.	++	Moderately treated
C. R.	+	Adequately treated
S. T.	+	Adequately treated
E. C.	+	Adequately treated
F. W.	+	Inadequately treated
S. L.	+	Moderately treated
F. B.	−	Adequately treated
W. O.	−	Adequately treated

The response is figured on the basis of +++++ as representing a complete response to irradiation.

In only 2 of the cases was a good response obtained to irradiation, and here the result left much to be desired. In 3 cases a moderately good response was obtained, in 4 cases a mild response, and in 2 cases no response of any significance was noted.

An analysis of some of the individual cases may be of value first before summarizing our opinions concerning the effect of irradiation on the medulloblastomas. If we take the 2 cases first which responded well, it is apparent that in both there were definite histological changes.

Case H. D. (Surg. No. 18736). *Medulloblastoma of the vermis and right cerebellum. Operation and partial removal. Five courses of irradiation with great relief. Final complete removal of tumor.*

History. This patient, a woman, aged thirty-eight, entered the University Hospital April 2, 1930, complaining of headache. The headache was occipital and despite a tonsillectomy became increasingly worse. She suffered also with dizziness and a tendency to sway to the right.

Neurological examination revealed right lateral nystagmus which was not constant, dyssynergia of the left arm, and difficulty in walking. There was 8D choking in the left eye and 4D in the right. The roentgen examination of the skull revealed nothing abnormal. A diagnosis of a left cerebellar tumor was made.

Operation. On April 27, 1930, Dr. Frazier performed a suboccipital craniectomy exposing a tumor in the left cerebellar hemisphere and in the vermis. A partial removal was made. Histological studies showed the tumor to be a medulloblastoma. The patient was discharged much improved June 13, 1930, after receiving a course of irradiation. Tumor dose 578 r, period nine days, λ effective 0.17 Å.

Second course of roentgen therapy September 16 to 26, 1930. Tumor dose 432 r, period ten days, λ effective 0.17 Å.

Third series of roentgen therapy December 29, 1930, to January 27, 1931. Tumor dose 1,084 r, period twenty-nine days, λ effective 0.17 Å.

Second Admission. The patient was readmitted October 10, 1932, for irradiation of the tumor and was discharged October 22, 1932, after its completion. Tumor dose 1,445 r, twenty-five days, λ effective 0.17 Å.

Third Admission. On April 30, 1934, the patient entered the hospital again with the story that she had had some recurrence of vomiting attacks, and a return of her occipital headache. She now showed a tendency to fall to the left, was unsteady in her gait, and could not walk a straight line without falling. She had a positive Romberg, and dyssynergia on the left side. There was no papilledema. After another course of irradiation she improved so much that most of her cerebellar disturbances disappeared. (Tumor dose 1,778 r, fifteen days, λ effective 0.17 Å.) There remained only a slightly inaccurate gait.

Fourth Admission. In July, 1934, the patient returned once more for study. Since discharge a few months before, she had had mild attacks of headache and nausea. Neurological examination again revealed dyssynergia of the left arm, a tendency to fall to the left, and inability to walk. Further irradiation was not possible at this time so another operation was performed.

Second Operation. On July 28, 1934, Dr. Frazier again explored the posterior fossa and removed all the tumor tissue in the cerebellum. She withstood the operation very well and was discharged much improved August 31, 1934.

This patient has subsequently received two more series of external irradiation with clinical improvement in symptoms. She is now alive, with symptoms, five years and six months since admission.

Histologic Studies:

Pre-irradiation Specimen (April 28, 1930). This is a typical medulloblastoma. It is very cellular. The tumor cells are often arranged

in streams. The nuclei are hyperchromatic and typically carrot-shaped. Mitoses are relatively infrequent.

Post-irradiation Specimen (July 28, 1934, two months after last roentgen therapy). Changes which might be attributed to the irradiation were seen in the tumor. The cells showed a tendency to pyknosis but no severe cellular changes were evident. The greatest change was seen in the stroma. There was more fibrous and reticular stroma than in the pre-irradiation specimen. The tumor structure was also much more distorted than in the original specimen.

Comment. The first specimen was a typical medulloblastoma. The histological specimen before irradiation was so characteristic that the diagnosis was made with little hesitancy despite the fact that it was found in a woman aged thirty-eight. The tumor was very cellular, and had no stroma except a very fine reticulum among the cells. The post-irradiation specimen, taken four years after irradiation was instituted, was totally different in appearance (Fig. 1). It contained many more vessels, and much more connective tissue stroma. The capillary structure of the tumor was much richer than in the first specimen. The tumor was very rich in capillaries and contained large cavernous spaces filled with blood. In contrast to the poor stroma structure of the first specimen, the second was very rich in stroma, especially along the edge of the tumor.

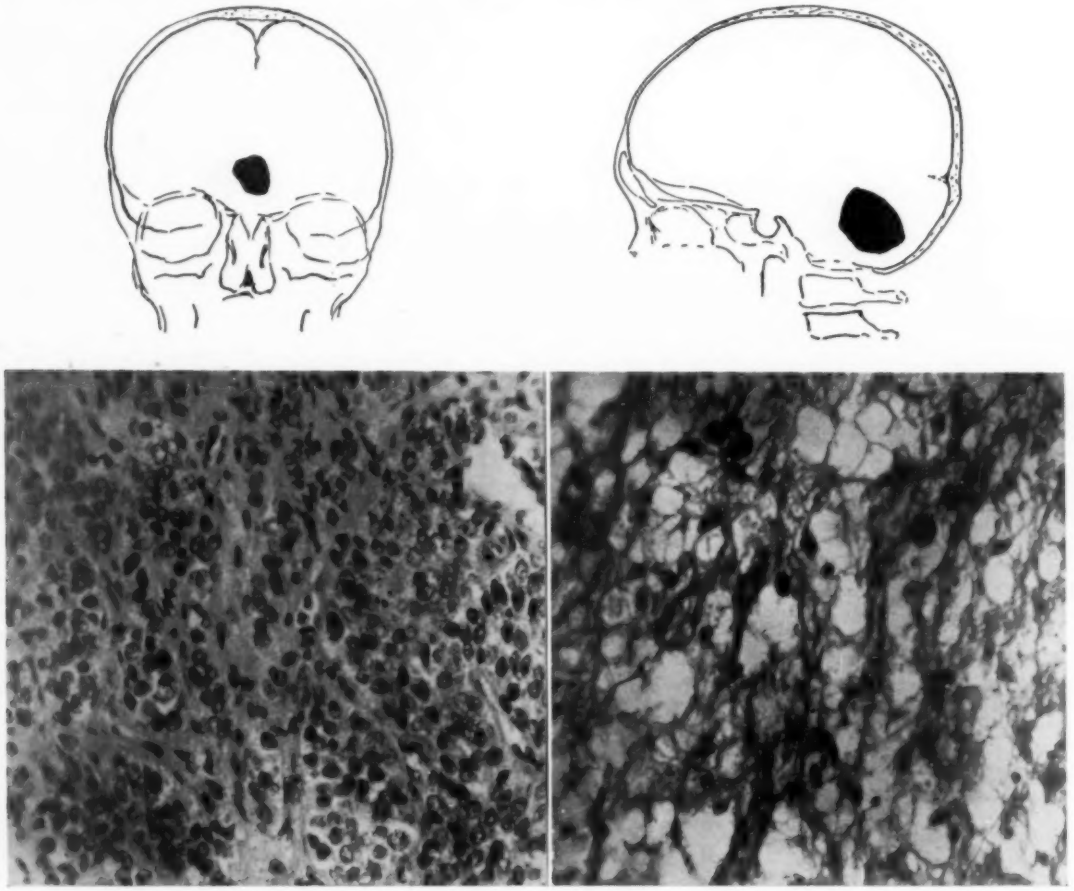


FIG. 1. Case H. D. Medulloblastoma of the cerebellar vermis and left cerebellar hemisphere. Tumor dose adequate. Series doses inadequate. Series interval too long. Marked histological effects. *Irradiation data:* Five series, period four years, tumor dose 3,792 r, λ effective 0.17 Å. *Pathology:* There is marked increase in neuroglia fibrils after irradiation (lower right).

Another adequately treated medulloblastoma with definite histologic changes is illustrated by the following case:

Case W. P. (Surg. No. 30038). *Medulloblastoma with single course of irradiation. Definite histologic changes in the tumor.*

History. The patient, a boy, aged thirteen, entered the University Hospital October 19, 1934, with headache, vomiting, and failing vision. He had been well until July, 1934, when he began to complain of early morning headache and vomiting. At the same time the vision became blurred and increased steadily to the time of admission. He became very somnolent in September, 1934. About the same time the gait became staggering and he was quite unsteady in his muscular acts.

Neurological examination revealed choked disc of 4D in the right eye and 3D in the left, a right external rectus weakness, impaired hearing in the left ear, unsteady station and gait with staggering to the left, dysmetria with the left arm. The roentgen examination of the head revealed signs of increased intracranial pressure.

Operation. On November 1, 1934, Dr. Frazier performed a suboccipital craniectomy and found a tumor invading the left cerebellar hemisphere. A specimen was removed for study.

Course. Following operation the patient made a good recovery. Irradiation of the tumor was given over a period of a month. Tumor dose 1,238 r, period thirty-two days, λ effective 0.17 Å. During this time the clinical condition improved but secondary optic atrophy developed with resultant loss of vision. The wound became quite tense at one time but this subsided with repeated ventricular taps. For a time the patient was able to get out of bed but he gradually failed and in April, 1935, became stuporous and died.

Necropsy revealed a very large glioma involving the vermis and the left cerebellar hemisphere, and filling the fourth ventricle.

Histologic Studies. The specimen was obtained four months after irradiation. There were distinct differences between the portions of tumor removed at the periphery and those in the center. The peripheral portions showed a tumor structure composed of much fibrous stroma with cells arranged in lobules surrounded by walls of fibrous tissue. The nuclei were pyknotic. Many of them were destroyed

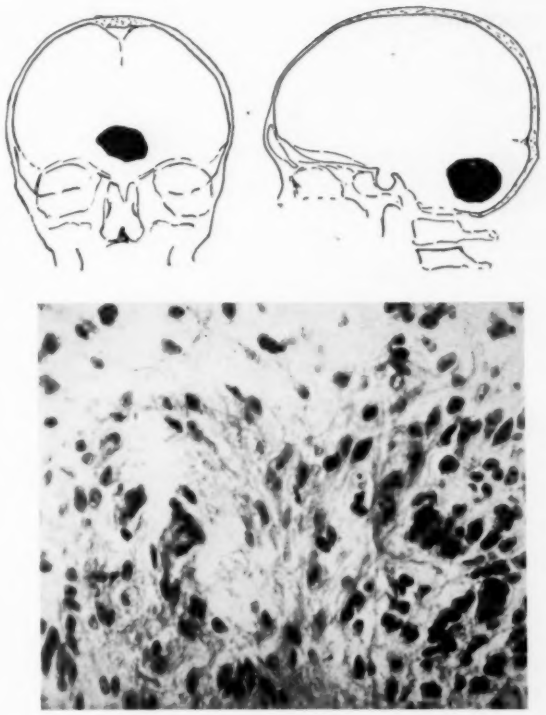


Fig. 2. Case W. P. Medulloblastoma of cerebellar vermis. Tumor dose inadequate. Series doses inadequate. Marked histological effects. *Irradiation data:* One series, period thirty-two days, tumor dose 1,238 r, λ effective 0.17 Å. *Pathology:* Note the great increase in fibrous stroma after irradiation.

and consisted of broken clumps of chromatin. Large vesicular nuclei were present as well as occasional multinucleated cells. There were numerous pseudomitoses. There was also a rich glial carpet among the cells. In the central portions the tumor structure was chiefly cellular, with a fine reticulum among the cells. This portion was a typical medulloblastoma.

Comment. In the second case, only one course of treatment was given, but this course was given over a period of a month so that a moderate amount of treatment was delivered to the tumor. No specimen was available for study before irradiation, but from our knowledge of the normal structure of these tumors it was apparent that there were definite changes in the tumor as a result of irradiation. One feature of particular interest is illustrated by this case: the fact that the changes at the periphery of the tumor were definitely

more marked than in its center. The central portion showed the typical structure of a medulloblastoma. At the periphery the tumor showed a varied appearance. There were areas in which the tumor structure was intact. There were many other areas in which cellular destruction was rife, as shown by the presence of large numbers of pyknotic, vesicular and multinuclear forms. There were many pseudomitoses. In addition, there was a rich stroma composed of collagen and glia fibrils (Fig. 2). This was in sharp contrast to the absence of stroma in the cell-rich central portion of the tumor. The stroma separated the tumor cells into small lobules completely surrounded by a wall of collagen.

Three cases of the medulloblastoma group responded moderately well to treatment. The following case illustrates a moderately well-treated medulloblastoma, as judged by the histologic changes:

CASE J. M. (Surg. No. 25655). *Left cerebellar medulloblastoma with extension into vermis. Relief for long periods after two courses of irradiation. Subsequent death. Definite changes in tumor attributed to irradiation.*

History. The patient, a male, aged twenty-four, was admitted to the University Hospital in the care of Dr. C. H. Frazier on November 14, 1932. He was well until August, 1932, when he experienced bilateral supraorbital pain. This was moderate in severity at first, but it later became very severe. He developed severe headache in October, 1932, and about the same time developed nausea and vomiting which always aggravated his headache. The headaches continued with unabated severity and three weeks before entrance he complained of stiffness in the neck. He had suffered from impaired vision for six months. For two weeks before entrance he was hypersomnolent.

Neurological examination revealed signs implicating the left cerebellar hemisphere. There was definite dysmetria on finger-nose test on the left. There was marked past pointing on the left side, and dyssynergia with the left arm and leg. Nystagmus was present and there was 2D of choking in each eye. The Bárány sign suggested a cerebellar lesion.

The blood and spinal fluid serology was negative. There was no roentgen evidence of increased pressure. There was no hemianopsia.

Suboccipital craniectomy on November 21, 1932, by Dr. C. H. Frazier, revealed an enlarged left cerebellar hemisphere but no attempt was made to remove the tumor at this sitting. Following operation the cerebellar signs improved markedly and he was discharged to return for removal of the tumor

Second Admission, February 13, 1933. For about one month after discharge the patient felt very well. He then developed headache and vomiting which persisted until his admission for the second time. The neurological signs were essentially the same as on first admission. Cerebellar signs were present, pointing to a left cerebellar hemisphere involvement. In addition, there seemed to be some weakness of the left side.

Second Operation, February 16, 1933. Dr. C. H. Frazier removed a large part of the tumor by the Bovie loop. The patient made a good recovery and left the hospital twelve days after operation.

Third Admission, March 29, 1933. The patient was readmitted one month after discharge for irradiation of the tumor which was diagnosed medulloblastoma. He received his first course of irradiation, and following this seemed to be improved. Tumor dose 832 r, thirteen days, λ effective 0.17 Å.

Second series of roentgen therapy, May 22 to June 22, 1933. Tumor dose 1,665 r, period thirty-one days, λ effective 0.17 Å.

Third course of roentgen therapy, October 2 to November 1, 1933. Tumor dose 1,665 r, period thirty days, λ effective 0.17 Å.

Fourth Admission, May 4, 1934. The patient felt well for a year and was able to do light work in a store. Because of recurrence of his headache he was again admitted for radiation therapy. He again showed definite left cerebellar signs. After another course of irradiation he again improved. Tumor dose 1,820 r, period nineteen days, λ effective 0.125 Å. He soon had a recurrence of his symptoms, however, and was admitted in August, 1934, for the last time.

Fifth Admission, August 1, 1934. On this admission Dr. Frazier performed another operation in which he exposed the right cerebellar hemisphere and removed tumor tissue from this area. The patient responded poorly to the operation and died the following day.

Necropsy revealed a large tumor in the left cerebellar hemisphere involving the entire

hemisphere except for a part of the left biventer. It invaded the vermis, the cerebellar nuclei, and the right cerebellar hemisphere. The tumor was soft, grayish-red, and in part necrotic. It was diagnosed medulloblastoma on histological study.

Histological Studies:

Pre-irradiation Specimen (November 21, 1932). This revealed a very cellular tumor in which the cells were arranged in streams and rows. For the most part the cells predominated by far over the interstitial tissue. However, a fine silver reticulum could be demonstrated and in addition occasional broad bands of collagen penetrated here and there into the tumor. Blood vessels were moderately numerous but showed no signs of pathological changes. The tumor nuclei were carrot-shaped. There were many oval, indented, and spindle-shaped forms. The cytoplasm could not be made out clearly. Mitoses were very numerous.

Post-irradiation Specimen (August 2, 1934). This was studied five months after the first course of irradiation and three months after the last roentgen treatment. It showed definite changes as compared with the non-irradiated specimen. (1) The cells, first of all, were often necrotic in large areas. There were portions of the tumor in which the cells were necrotic and took no stain whatever. In adjacent portions of the tumor, however, there were large groups of cells which seemed to be very healthy. There were many so-called pseudomitoses in the tumor. These consisted of nuclei with large irregular clumps of chromatin which appeared to be mitoses but which, in reality, represented cells which had undergone necrosis. The figures formed by the chromatin clumps did not correspond to mitotic figures of any known sort. (2) There was definitely more stroma in the second specimen. There were many more fingers of connective tissue extending out into the tumor. There was also an increase in the delicate reticular tissue among the cells. The interfibrillar tissue was also increased. In fact, none of this tissue was seen in the pre-irradiation specimen. In the post-irradiation specimen there were numerous straight, fine, hard fibrils arranged in parallel rows, which stained with phosphotungstic acid, hematoxylin and with silver stains. Their exact nature is not clear, but it may be that they were fibroglia. (3) The vessels in this post-irradiation specimen were definitely thickened due to proliferation of the cells in the vessel walls.

Comment. There is one other feature of the irradiation which is very important: there was a definite difference between the histological characteristics of the tissue removed from the outer and inner portions of the tumor. The outer portion revealed definite changes which could be attributed to irradiation. The inner portions of the tumor revealed uniformly healthy cells with none of the changes just described.

This case showed moderate changes at the periphery of the tumor and little if any changes in its central portion. The periphery revealed a marked distortion of the cellular structure. There were large areas in which the cells stained poorly and the nuclei were disintegrated. Side by side with these were other areas in which the tumor cells were flourishing. In addition, there were large fingers of collagen stroma penetrating among the cells, and a definite increase in the amount of intercellular fibrillary tissue as compared with that seen in the more normal portions of the tumor. In the other two cases the changes were not so pronounced and consisted largely of pyknotic changes in the nuclei with some increase in the stroma.

Five cases responded only mildly to irradiation. This type of reaction is illustrated by the following case:

Case P. H. (Surg. Nos. 10922, 11572, 11998, 12483, 18126). *Medulloblastoma of the vermis and right cerebellar hemisphere. Four courses of irradiation with improvement. Moderate histologic changes in the tumor.*

History. The patient, a woman, aged thirty-eight, entered the University Hospital for the first time May 18, 1927. She developed severe, continuous occipital headaches five weeks before entrance. Nausea and vomiting accompanied the headache. For three weeks she had had pain over the right eye. For four weeks before admission she had been confined to bed because of dizziness whenever she attempted to rise.

Neurological examination revealed bilateral choked disc of 5D on the right and 4D on the left. There was a slight paresis of the right external rectus. The right hand was dyssynergic. There was considerable truncal dys-

synergia, and persistent dysmetria with the right hand.

Ventriculogram was taken on May 28, 1927, by Dr. F. C. Grant. It revealed a moderate degree of internal hydrocephalus. This was followed by a

Suboccipital craniectomy on June 21, 1927, by Dr. Frazier. The right cerebellar hemisphere was definitely enlarged pushing the midline structures over to the left. No tissue was removed.

Second Admission. On August 24, 1927, the patient was readmitted for irradiation of the tumor. She had had very little headache or dizziness since discharge and felt greatly improved. She was given a course of irradiation and improved after this. Tumor dose 784 r, period twelve days, λ effective 0.17 Å.

Third Admission. The patient was admitted again on October 25, 1927, for irradiation of the tumor. She had been entirely symptom-free since discharge and showed a few evidences of cerebellar involvement on examination. The fundi showed subsidiary choked disc with atrophy. Tumor dose 784 r, period thirteen days, λ effective 0.17 Å.

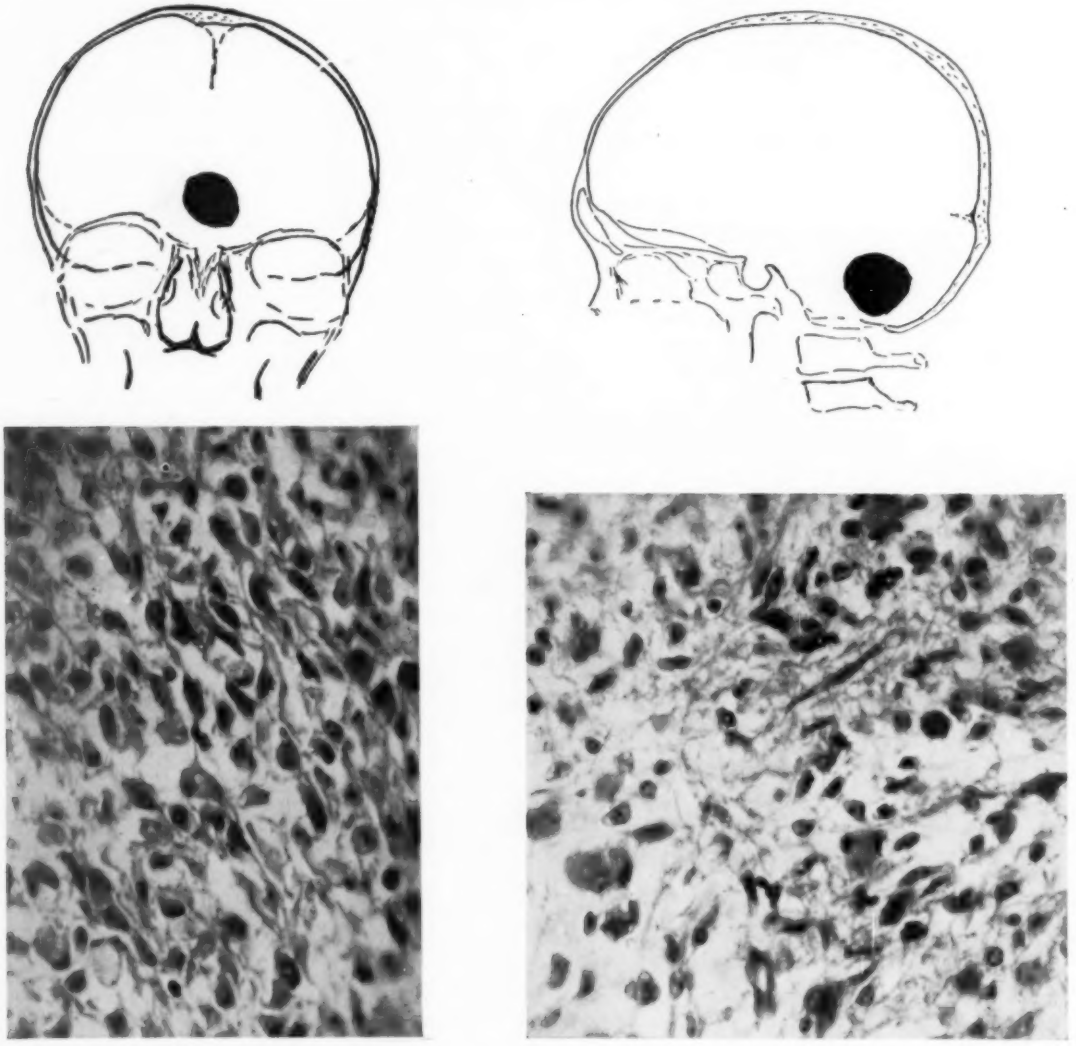


FIG. 3. Case P. H. Medulloblastoma of cerebellar vermis. Tumor dose adequate. Series doses inadequate. Series interval too long. Moderate histological effects. *Irradiation data:* Three series, period five months, tumor dose 2,457 r, λ effective 0.17 Å. *Pathology:* The increase in stroma and the fewer cells are apparent. Note the plump cells in the post-irradiation specimen (lower right).

Fourth Admission. Irradiation was again given on January 4, 1928. She continued to improve except for occasional pain over the right eye and slight unsteadiness in gait. Tumor dose 1,040 r, period sixteen days, λ effective 0.17 Å.

Fifth Admission. The final admission was February 13, 1930. About one year after completion of her last course of irradiation she noticed a bulging of her suboccipital craniectomy wound. At first this subsided and reappeared, but it had persisted for a month before admission and necessitated hospitalization. It is of interest to note that two years had passed since her last course of irradiation. The cerebellar signs were the same as on the first admission and indicated a tumor in the right cerebellar hemisphere. There was no choked disc.

Second Operation. On February 28, 1930, Dr. Frazier removed practically the entire right cerebellar hemisphere which was entirely invaded by tumor. Following operation, the patient developed a spinal fluid leak and died.

Necropsy revealed a large tumor involving the entire cerebellar vermis and extending into both cerebellar hemispheres.

Histologic studies (twenty-five months after the last irradiation) revealed a medulloblastoma. There was evidence of extensive damage by irradiation (Fig. 3). The cells were pyknotic, shrunken, and often sclerosed. Side by side with them were other cells which appeared quite healthy. The vessels showed endothelial proliferation, sometimes with complete occlusion of the vessel. Connective tissue stroma was quite abundant throughout the tumor in the form of long prolongations everywhere. Pseudomitoses were numerous.

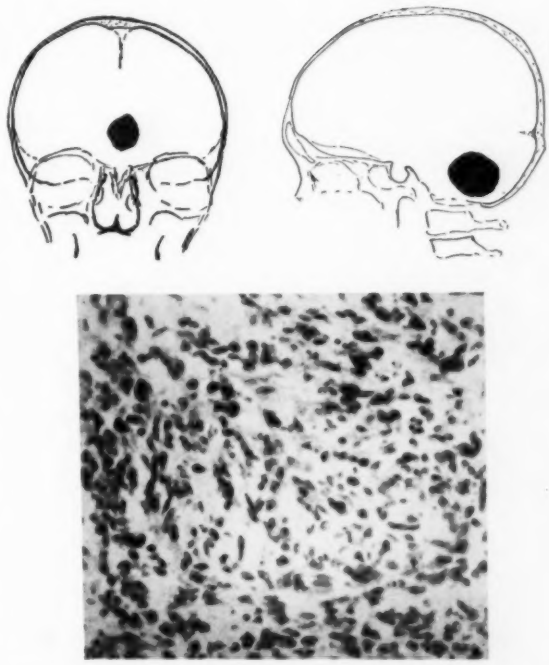


FIG. 4. Case F. W. Medulloblastoma of cerebellar vermis. Tumor dose inadequate. Mild histological effects. *Irradiation data:* One series, period three days, tumor dose 130 r, λ effective 0.17 Å. *Pathology:* Even under low power there may be seen numerous pseudomitoses or disintegrated nuclei.

TABLE IV

INTERVAL BETWEEN TREATMENT AND POST-IRRADIATION BIOPSY OR NECROPSY

Case	Type of Tumor	Interval between Treatment and Biopsy or Necropsy	
		First treatment to biopsy	Last treatment to biopsy
J. L.	Medulloblastoma	5 mo.	4½ mo.
P. H.	Medulloblastoma	30 mo.	25 mo.
C. R.	Medulloblastoma		
E. C.	Medulloblastoma	15 mo.	3 mo.
J. M.	Medulloblastoma	16 mo.	3 mo.
S. T.	Medulloblastoma	21 mo.	10 mo.
F. W.	Medulloblastoma	5 days	2 days
S. L.	Medulloblastoma	34 days	16 days
F. B.	Medulloblastoma		
W. P.	Medulloblastoma	5 mo.	4 mo.
W. O.	Medulloblastoma	8 mo. before 1st biopsy 5 yr. before 2nd biopsy	3 mo. before 1st biopsy 20 mo. before 2nd biopsy
H. D.	Medulloblastoma	48 mo.	2 mo.

The histologic changes were indicative of damage to the tumor of a moderate degree by irradiation.

These showed for the most part scattered changes in the tumor cells illustrated by pyknosis, pseudomitoses, and vacuolization of the nuclei. There were minor changes in the stroma seen by a mild proliferation of collagen tissue. In one case there were beginning hyaline changes in the stroma.

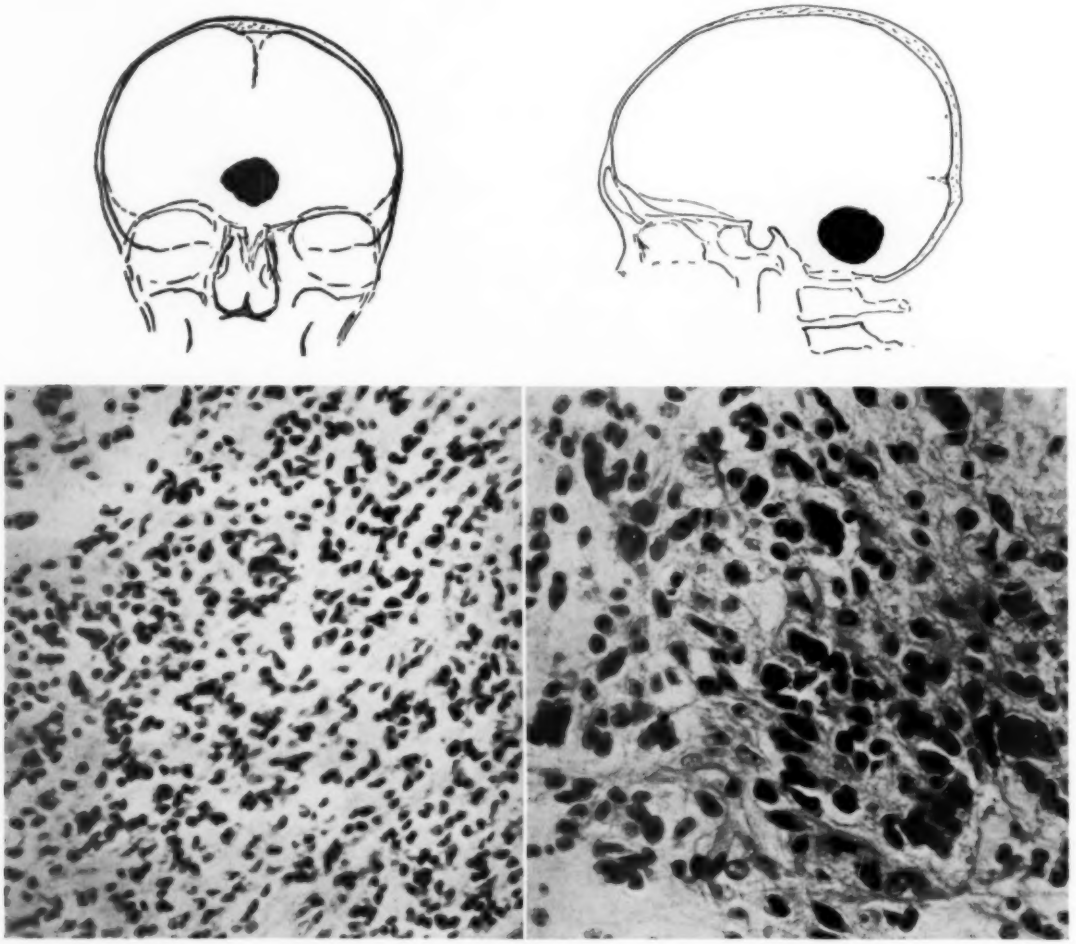


FIG. 5. Case S. T. Medulloblastoma of cerebellar vermis. Tumor dose adequate. Series doses inadequate. Series interval too long. Mild histological effects. *Irradiation data:* Four series, period ten months, tumor dose 3,811 r, λ effective 0.17 Å. *Pathology:* Note the great increase in stroma and the decrease in cellularity.

Summary of Histological Effects of Irradiation. Of the 12 medulloblastomas studied before and after irradiation, 5 showed either a moderate or marked response to irradiation, 5 showed a mild response, and 2 no response at all. The reasons for the variation in response are due in part to the extreme irregularity in the intervals between the treatment and the procuring of a biopsy. Reference to Table IV will demonstrate clearly that there was wide variation in this respect, and hence a great difference in the tissue response.

The changes were visible largely in the cells. These were of various types. In cases recently irradiated the nuclei were seen in various stages of disintegration. The chromatin was broken into coarse clumps which gave the appearance of mitoses, but in

reality were not mitoses. These figures we have referred to as pseudomitoses (Fig. 4). They are found in biopsy specimens removed soon after irradiation, and disappear in later specimens. In other specimens, the nuclear changes consisted of pyknosis, or less commonly of vacuolization or fatty degeneration. Occasionally the nuclear response was seen in a necrosis evidenced by a loss of the staining properties of the cells which appeared like shadow cells. In some cases there were fewer mitotic figures after irradiation, but in most instances there was no great change after irradiation.

Next to the cells, the structure which showed most change was the connective tissue stroma. In 8 of the 12 cases the stroma was definitely increased in the tumor after irradiation (Figs. 5 and 6). The increase was noted around the vessels, and among the cells. Most of it had no relation to the vessels. The stroma seen among the cells was composed of collagen which was found in broad bands in some tumors, and of a fine reticular structure which seemed to be more pronounced after irradiation in several of our tumors.

Relatively few changes were found in the vessels themselves. In a few cases, there was proliferation of the vascular endothelium and in an occasional instance adventitial thickening. In only one case was fat found in the blood vessel wall.

In a few cases, there was an increased amount of necrosis in the tissue after irradiation. Since necrosis is not a very common feature of these tumors, it is of significance in these cases.

To summarize, we may state definitely that the medulloblastomas are radiosensitive. Changes are visible in these tumors both soon after irradiation and as a late effect. The changes are seen chiefly in the cells and fibrous stroma, and to a lesser degree in the vessels. While these tumors are radiosensitive, in no instance have we found them completely or even nearly completely destroyed by irradiation. On the contrary, if we were to estimate in quantitative terms the amount of tumor tissue

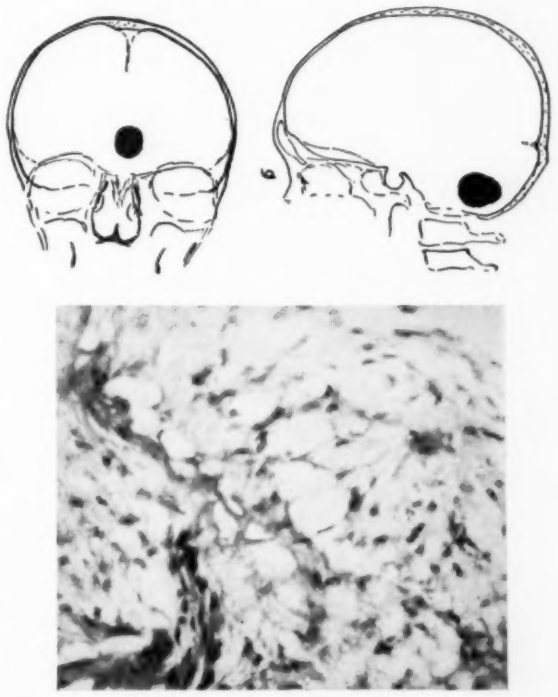


Fig. 6. Case E. C. Medulloblastoma of the cerebellar vermis. Tumor dose adequate. Series doses inadequate. Series interval too long. Mild histological effects. *Irradiation data:* Five series, period one year, tumor dose 5,222 r, λ effective 0.17 Å. *Pathology:* Note the marked increase of stroma after irradiation.

affected by irradiation, we would estimate only one-fourth or one-fifth as being affected by irradiation, and even this is a generous estimate. It is characteristic of the histological studies of these tumors after irradiation, that side by side in the same field are dead and living cells. While medulloblastomas, therefore, are radiosensitive, they have not as yet been destroyed by irradiation. The reasons for this must come from the radiologist.

That treatment as it is administered at the present time is inadequate is illustrated by the fact that complete inhibition of tumor cell growth has never been attained in a tumor which is radiosensitive. But that there is hope for the future treatment of such cases is also illustrated by the fact that the periphery of a few tumors in our series was quite seriously damaged by irradiation, resulting in a marked distortion

of tumor structure and a severe inhibition of tumor growth. This was in contrast to the few changes in the more central portions of the specimens. It seems logical to assume, therefore, that if irradiation can be administered sufficiently often and in sufficiently strong doses, greater effects may be expected from this form of treatment. Another point of value for future guidance in the treatment of medulloblastomas is found in the fact that cases clearly the extreme irregularity in the spacing of the treatments. Obviously this must be changed if optimum results are to be expected.

Analysis of Irradiation Data in the Medulloblastomas. It has now been shown that the medulloblastomas as a group are influenced by irradiation. If the radiologist has any place in the therapy of the gliomas, it should be in this group. The cells of these tumors, however, do not exhibit a homo-

Table V

INTERVAL BETWEEN SERIES OF THE MEDULLOBLASTOMA GROUP

Case	No. Series	Interval between Series				
		1st to 2nd	2nd to 3rd	3rd to 4th	4th to 5th	5th to 6th
J. L.	1					
P. H.	3	8 wk.	10 wk.			
C. R.	5	9 wk.	9 wk.	15 wk.	14½ wk.	
J. M.	4	7 wk.	17 wk.	7 mo.		
S. T.	4	10 wk.	14 wk.	4 mo.		
F. W.	1					
S. L.	1					
F. B.	3	9 wk.	9 wk.			
W. P.	1					
W. O.	9	12 wk.	8 wk.	5 mo.	18 mo.	7 mo. 5 mo. 1 mo. 4 mo.
E. C.	5	3½ mo.	3 mo.	10 wk.	3 mo.	
H. D.	6	14 wk.	14 wk.	22 mo.	19 mo.	14 mo.

which have been studied within a few days after the cessation of irradiation show much more evidence of cell death than those treated some time past. These dead cells are probably crowded out by the rapidly multiplying cells of the tumor and little evidence is seen of them later. Sufficient therapy must be given, therefore, to maintain the level of cell death above that of cell proliferation. If this can be attained we shall have reached our first goal in the conquest of the medulloblastomas. Finally, in order to obtain the maximum benefit from irradiation, it seems clear that treatments must be given at regular intervals. Possibly one of the reasons why better results were not obtained in treatment is shown by a study of Table v which shows

geneous response. Some are readily destroyed by minimal quantities of irradiation, while others continue to live, divide and form new cells to replace those destroyed. This histological evidence is strongly supported by the belief that these tumors have a tendency to recur following treatment.

This tendency to recur histologically must be considered in analyzing the irradiation data. If one considers only the total tumor dose delivered, it is difficult to draw any conclusions because the effect of the first series of irradiation may have been completely or partially obliterated (Table vi). We believe that such regeneration is probable because of the comparatively small amount of irradiation delivered dur-

Table VI

Case	Total Tumor Dose	Number of Series	Time of First Treatment to Biopsy	Response
H. D.	3,792 r	4	50 mo.	+++
W. P.	1,238 r	1	5 mo.	+++
J. M.	5,980 r	4	16 mo.	++
P. H.	2,457 r	3	30 mo.	++
J. L.	1,042 r	1	5 mo.	++
C. R.	5,640 r	5		+
S. T.	3,811 r	4	24 mo.	+
E. C.	5,222 r	5	15 mo.	+
F. W.	130 r	1	5 days	+
S. L.	1,445 r	1	3 mo.	+
F. B.	3,395 r	3		−
W. O.	2,704 r	4	48 mo.	−

Table VII

Case	Average Tumor Dose per Series in r	Average Time between Series in Months	Response
H. D.	948	12	+++
W. P.	1,238	—	+++
J. M.	1,495	4	++
P. H.	819	1.5	++
J. L.	1,042	—	++
C. R.	1,128	2.5	+
S. T.	452	2.5	+
E. C.	1,044	2.5	+
F. W.	130	—	+
S. L.	1,445	—	+
F. B.	1,131	2	−
W. O.	676	3	−

ing each series and the irregular and often lengthy time interval between them (Table VII).

If one considers only the last series of treatment (i.e., preceding removal of the biopsy specimen), it is readily seen that with the exception of 2 cases there is a fairly accurate correlation between intensity of irradiation and tissue response (Table VIII). The 2 cases which are not in accord with this reasoning must be explained in some other way, possibly on the basis of inherent biological quality or physiological status at the time of irradiation. One of these cases (F.W.) showed an extreme degree of radiosensitivity, while the other (S.L.) exhibited a more resistant architecture.

From the data presented, we are convinced that this group of cases has been under-irradiated. We believe that this is true particularly from the standpoint of the quantity delivered during each series and the interval between the respective series. Clinical experience has indicated also that these patients do not, as a rule, get as much benefit from the fourth or fifth series as they obtained from the first. Something has happened in the tumor cells which decreases their sensitivity. This "tolerance" to irradiation has also been noted by others (Bailey, Sosman and Van Dessel[2]). Should this not be another reason for delivering the maximum amount of ir-

Table VIII

Case	Total Tumor Dose—All Series	Tumor Dose—Last Series	Series Duration	Interval to Biopsy	Response
H. D.	3,792 r	1,778 r	15 days	2 mo.	+++
W. P.	1,238 r	1,238 r	32 days	4 mo.	+++
J. M.	5,980 r	1,820 r	19 days	3 mo.	++
P. H.	2,457 r	1,042 r	16 days	25 mo.	++
J. L.	1,042 r	1,042 r	10 days	5 mo.	++
C. R.	5,640 r	784 r	10 days	None	+
S. T.	3,811 r	1,042 r	12 days	14 mo.	+
E. C.	5,222 r	1,042 r	10 days	3 mo.	+
F. W.	130 r	130 r	3 days	2 days	+
S. L.	1,445 r	1,445 r	18 days	17 days	+
F. B.	3,395 r	784 r	7 days	None	−
W. O.	2,704 r	676 r	4 days	3 yr.	−

TABLE IX

RESPONSE OF GLIOBLASTOMA MULTIFORME TO IRRADIATION

Case	Degree of Response	Irradiation
H. B.	+	Adequately treated
R. A.	+	Adequately treated
E. D.	+	Adequately treated
H. D.	+	Adequately treated
E. J.	−	Moderately treated
C. W.	−	Moderately treated
A. J. R.	−	Inadequately treated

radiation during the first series of treatment? While we do not believe that one is justified at this time in presenting a definite and fixed set of irradiation standards for the medulloblastomas, it is our opinion that the therapy should be planned to destroy the most radioresistant cells, and to inhibit, as far as possible, cell regeneration. This can only be attained (1) by using the maximum number of skin portals, (2) by treating each portal to the limit of skin tolerance, (3) by maintaining the shortest possible interval between series of treatments.*

GLIOBLASTOMA MULTIFORME

Seven tumors of this type were studied both before and after irradiation. The results are summarized briefly in the following table (Table IX).

The histological changes following irradiation are particularly difficult to evaluate in this type of tumor because of the fact that the tumor structure may vary so widely in different portions of the tumor, and also because this type of tumor in the course of its development may undergo changes similar to those which might be attributed to irradiation. For example, it is not unusual to find a tumor of this type entirely necrotic, with hardly a solid area left from which to make a diagnosis. It might easily be inferred that much of this necrosis was due to irradiation if the patient had received such therapy. One must be particularly cautious, therefore, in drawing conclusions concerning the efficacy of irradiation in this tumor group.

TABLE X

INTERVAL BETWEEN TREATMENT AND POST-IRRADIATION BIOPSY OR NECROPSY IN THE GLIOBLASTOMA MULTIFORME GROUP

Case	Interval between Treatment and Biopsy or Necropsy	
	First treatment to biopsy	Last treatment to biopsy
H. B.	4 mo.	3 mo.
R. A.	20 mo.	9 mo.
H. D.	3 mo.	2½ mo.
C. W.	3½ mo.	3 mo.
A. J. R.	6 days	1 day
E. J.	5 mo.	2½ mo.
E. D.	29 mo.	12 mo.

From the radiation standpoint 4 of the 7 cases were adequately treated, 2 were

TABLE XI

INTERVAL BETWEEN SERIES OF THE GLIOBLASTOMA MULTIFORME GROUP

Case	No. Series	Interval between Series			
		1st to 2nd	2nd to 3rd	3rd to 4th	4th to 5th
H. B.	1				
R. A.	4	7 wk.	5 mo.	3½ mo.	
H. D.	1				
C. W.	1				
A. J. R.	1				
E. J.	2	8 wk.			
E. D.	5	8 wk.	3 mo.	10 mo.	6 wk.

* Patients with a medulloblastoma are routinely given irradiation over the spinal cord and cerebral hemispheres because of the possibility of transplants in these regions. Our observations, however, are confined to the primary tumor.

moderately well treated, and 1 was inadequately treated. Histologically speaking, however, only 4 of the tumors revealed a response and this was only of a mild degree. Three revealed no effects whatever from irradiation.

In 2 cases which showed an effect from irradiation, the changes were slight but definite. This is seen in the following case:

Case H. B. (Surg. No. 30939). *Glioblastoma multiforme with one course of irradiation. Minor changes in post-irradiation specimen.*

History. The patient, a male, aged forty-four, was admitted to the University Hospital on March 15, 1935, in the care of Dr. C. H. Frazier. In November, 1934, he developed severe headache and fell unconscious to the floor. He was unconscious for 1½ hours and awoke fairly clear. Following this, he had attacks of severe intermittent headache without loss of consciousness. In January, 1935, he developed persistent vomiting.

Neurological examination revealed 4D of choking in the right eye, and 5D in the left. There was weakness of the right arm, and a mixed motor and sensory aphasia. The visual fields showed nothing definite.

Operation on March 30, 1935. Dr. C. H. Frazier performed a left frontal craniotomy and found a tumor in the posterior part of the left temporal lobe. The tumor was adherent to the dura. It was soft, grayish in color and measured 4×5 cm. It was moderately well defined on the surface but definitely infiltrating in the depths of the tumor. He was discharged April 12, 1935, in good condition.

Second Admission. The patient was well following operation. He gained 16 lb., was mentally clear and had no aphasia. He was given radiation treatment from May 18 to June 17, 1935. He was in good condition at this time. Tumor dose 2,365 r, period twenty-nine days, λ effective 0.125 Å.

Third Admission. He returned on September 11, 1935. He had been well until July, 1935, when he had a sudden attack of headache and partial loss of consciousness lasting two hours. Following this he had frequent headaches, decreasing vision, and aphasia. Examination at this time revealed mental changes with disorientation, loss of memory, a motor and sensory aphasia, and weakness of the right hand. There was an incomplete right homonymous hemianopsia. No papilledema was found on this examination.

Second Operation. On September 18, 1935, the patient was again operated on by Dr. R. A. Groff. Only part of a recurrent tumor was removed, and the patient made a satisfactory recovery. He was discharged from the hospital October 8, 1935.

Histological Studies: Pre-irradiation Specimen (March 30, 1935). The tumor is quite necrotic. It has many cells which vary widely in appearance. The cells are arranged in lobules and streams; in some parts the tumor has a myxomatous appearance. Blood vessels are numerous. The cells tend to be bipolar. Giant cells are seen occasionally. Mitoses are numerous.

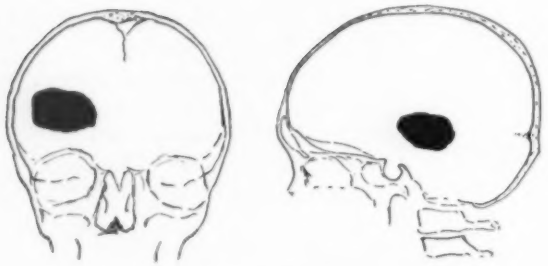
Post-irradiation Specimen (September 19, 1935, three months after the last roentgen treatment). There are a few changes in this specimen which might be attributed to irradiation: (1) there is an increase in the intercellular fibrils. Many more glia fibrils are seen among the cells than is usual in this type of tumor; (2) fewer mitoses are visible; (3) more marked changes in the blood vessels. Proliferative changes seem to be more pronounced and more widespread.

Comment. In this case, there was a marked cellular necrosis with large areas of the tumor staining poorly. There was in addition a definite increase in the amount of stroma present in the specimen studied after irradiation. The pre- and post-irradiation specimens differed definitely in their structure.

More marked changes were seen in the following case which also showed the effects of irradiation:

Case R. A. (Surg. Nos. 7656, 8302, 9286, 9998, 11969). *Glioblastoma multiforme in right frontal lobe. Four courses of irradiation. Moderate but definite changes in tumor after irradiation.*

History. This patient, a woman, aged thirty-five, entered the University Hospital February 8, 1926, in the care of Dr. C. H. Frazier. Ten years before admission she developed generalized headaches with some nausea and vomiting. They continued for a year and were then relieved. Four years later the symptoms recurred and persisted to the time of entrance. In the



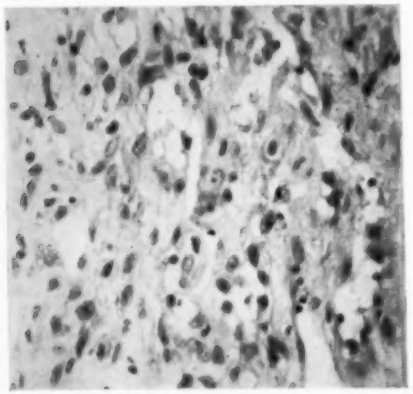


FIG. 7. Case H. B. Glioblastoma multiforme of the left temporal lobe. Tumor dose adequate. Mild histological changes. *Irradiation data:* One series, period twenty-nine days, tumor dose 2,365 r, λ effective 0.125 Å. *Pathology:* The cells appear more benign and the stoma is more abundant after irradiation.

past year there had been some failure of eyesight. For a few months before entrance she had noticed gross tremors of her right arm and leg. Recently she had observed that she could not understand spoken language as well as formerly.

Neurological examination revealed a lethargic, mentally clouded person with a spastic weakness of the right arm and leg and gross tremors of these members, especially of the arm. Smell was lost on the left side. There was a temporal cut in the left visual field. The fundi showed 4D choking on the right side and 3D on the left. The tendon reflexes were bilaterally exaggerated, more on the right than on the left. There was a suggestion of sensory aphasia.

The spinal fluid pressure was 14 mm. Hg. There was atrophy of the dorsum sellae.

Operation. On February 19, 1926, Dr. F. C. Grant made a ventriculogram which disclosed a large right frontal lobe tumor. On elevation of a right frontotemporal bone flap, a large gliomatous cyst was found and evacuated. About 50 c.c. of fluid was removed, and a hard nodular tumor was palpated in the tumor wall. Roentgen therapy was given March 3 to 15. Tumor dose 692 r, period twelve days, λ effective 0.17 Å. She was discharged April 1, 1926, in good condition.

Second Admission. The patient was quite well after operation. She returned on May 11, 1926, for radiation therapy which was completed May 21, 1926. Tumor dose 692 r, period ten days, λ effective 0.17 Å. At this time, the fundi showed no choking and there were no neurological findings of note.

Third Admission. The patient was readmitted October 5, 1926, for irradiation and discharged in good condition on October 17, 1926. Tumor dose 692 r, period eleven days, λ effective 0.17 Å. There had been no progression of her symptoms in the meantime.

Fourth Admission. A fourth course of irradiation was given from January 18, 1927, to February 3, 1927. Tumor dose 810 r, period sixteen days, λ effective 0.17 Å. The patient was in good condition and showed no signs of progess of the tumor.

Fifth Admission. She was again admitted to the hospital on October 21, 1927. She had been well apparently until a month before her final admission, when she noticed swelling of her area of decompression. She had struck her head a few months previously. Neurological examination at this time revealed a slight dysmetria of the left hand with left lower facial and left arm weakness. She had a left homonymous hemianopsia, 2D of choking in each eye, and a spinal fluid pressure of 20 mm. of mercury.

Second Operation. On November 3, 1927, Dr. W. J. Gardner again evacuated the frontal lobe cyst, removing 30 c.c. of clear and 30 c.c. of bloody fluid. She did well for a week, then developed an acute collapse and died.

Necropsy revealed a tumor of the right frontal lobe. It was diagnosed glioblastoma multiforme by Dr. N. W. Winkelman.

Histological Studies:

Pre-irradiation Specimen (February 19, 1926). Only a small bit of tissue was available for study. It showed a moderately cellular tumor with many vessels with thickened walls. The cells were astrocytic and lay in a rather dense carpet of glia fibrils. Multinucleated forms were seen here and there in some parts of the tumor and in others were quite numerous. Large astrocytic forms were present.

Post-irradiation Specimen (November 17, 1927, nine months after the last roentgen treatment). This showed some changes from the pre-irradiation specimen, but they were not very striking. (1) The staining quality of the cells was distinctly changed. Most of the cells took a much poorer stain than normal, but there were still parts of the tumor which seemed to stain normally; (2) there were fewer giant multinucleated forms. This was true of all parts of the tumor, a careful search revealing very few giant cells; (3) the interstitial tissue was greatly increased in amount. There was much more fibrous tissue both around the vessels and in the tumor, and there was also a definite increase in the amount of glial fibrils.

The pre-irradiation specimen was a typical glioblastoma multiforme with much polymorphism, many multinucleated cells, a fine reticulum, and no coarse collagen bands in the tumor structure. The specimen after irradiation showed definitely poorer staining quality of the cells, with large areas staining poorly and with many necrotic nuclei. There were fewer multinucleated cells, the difference between the two specimens being quite striking in this respect. The stroma was definitely increased in this specimen. This was of two sorts: (1) collagen stroma which was present in large amounts in the tumor after irradiation, and (2) glia fibrils which were also present in greater numbers after treatment.

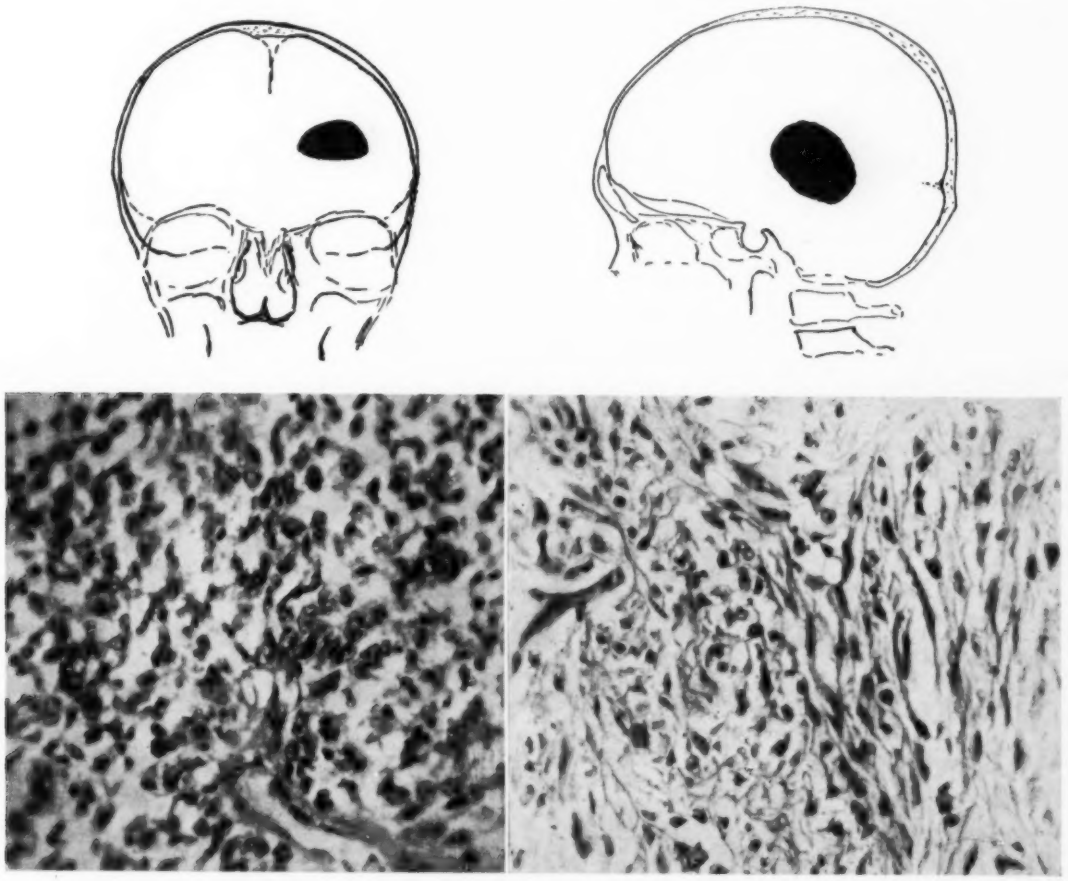


Fig. 8. Case R. A. Glioblastoma multiforme of the right temporal area. Total tumor dose adequate. Series doses inadequate. Mild histological effects. *Irradiation data:* Four series, period eleven months, tumor dose 2,598 r, λ effective 0.17 Å. *Pathology:* Note the great increase in stroma after irradiation (lower right).

Summary of Histological Findings. Only 4 of the 7 cases of glioblastoma multiforme revealed changes which could be attributed to irradiation. The changes were not pronounced, and might even be attributed to

the natural growth of the tumor. We are inclined, however, to regard them as being produced by the irradiation.

The cellular changes observed in the 4 cases which showed some response to irradiation consisted of (1) the development of pseudomitoses in 2 cases in which biopsy was available soon after irradiation; (2) a definite decrease in the number of giant cells in the post-irradiation specimen in 2 cases; this difference was so marked as to be very striking; (3) widespread cell necrosis in one case, as seen by the decreased staining properties of the cells which had undergone incomplete necrosis.

In 3 of the 4 cases there was an increase in the fibrous stroma (Figs. 7, 8 and 9). This was quite marked in one case. There were no visible changes in the vessels.

The glioblastoma multiforme group is slightly sensitive to irradiation. There are some changes which are attributable to the effects of irradiation. While they are not marked, they indicate at least that there is some susceptibility of the tissue and that irradiation as an adjunct to surgical treatment may be of some value. Tumors of this group vary widely in their cellular

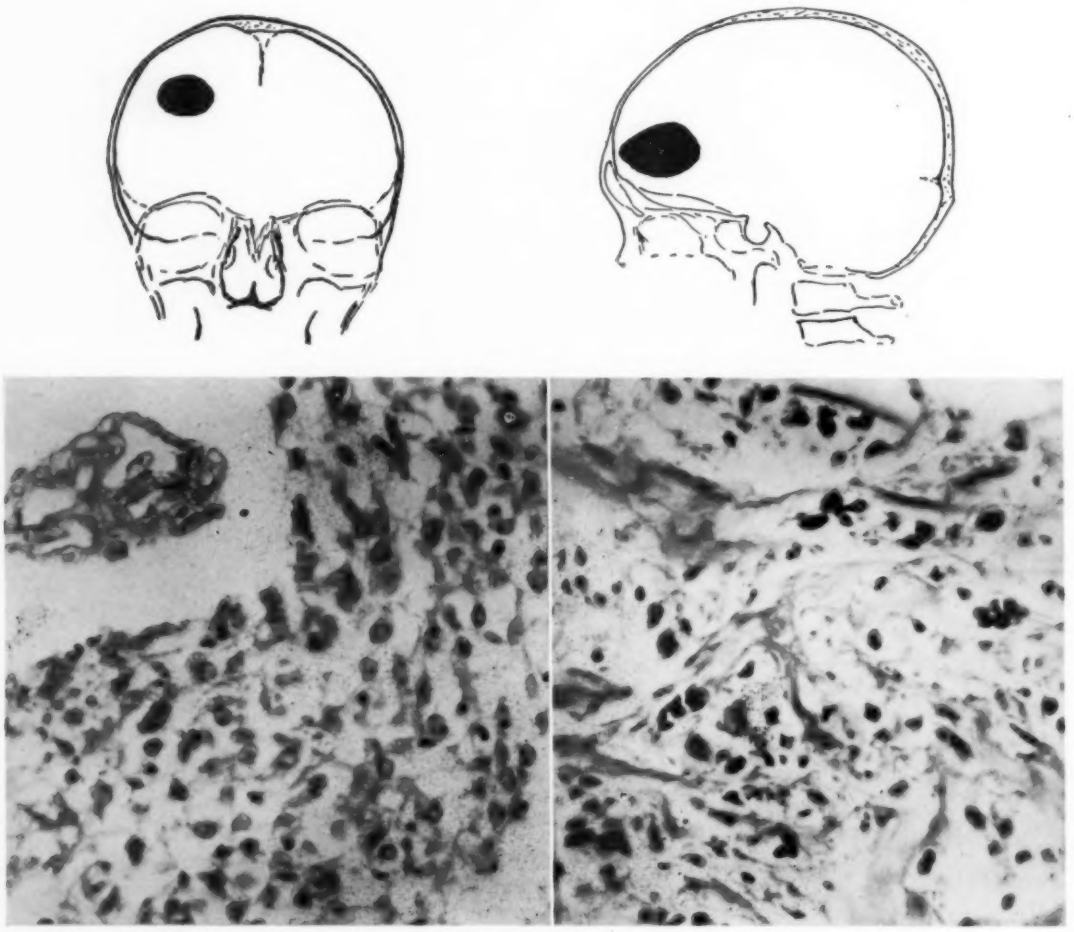


FIG. 9. Case E. D. Glioblastoma multiforme of left frontal lobe. Total tumor dose adequate. Series doses inadequate. Time interval correct. Mild histological changes. *Irradiation data:* Five series, period one year seven months, tumor dose 3,096 r, λ effective 0.17 Å. *Pathology:* Vascular proliferation, increase in fibrous stroma, and reticulin are seen in this tumor after irradiation.

structure and contain many different types of cells. It is to be expected therefore that irradiation will affect only some cells in these tumors.

Analysis of Irradiation Data of the Glioblastoma Multiforme. In this group of tumors the quantity of radiation delivered into the tumor parallels fairly closely the histological changes attributed to the effect of the roentgen rays. All of the patients who were classed as well treated (according to our arbitrary standards) showed mild irradiation changes. Two of these had only one intensive series of irradiation, the other 2 cases had less intensive treatment at intervals of two to eleven months. The cases which received a total tumor dose less than 2,000 r showed no irradiation effect (see Table XII).

ASTROCYTOMAS

Six astrocytomas were available for study. Both pre- and post-irradiation specimens were available.

TABLE XIII

RESPONSE OF ASTROCYTOMAS TO IRRADIATION

Case	Degree of Response	Irradiation
A. H.	+++	Adequately treated
E. L.	+++	Adequately treated
R. L.	++	Adequately treated
M. N.	–	Inadequately treated
H. K.	–	Adequately treated
F. L.	–	Moderately treated

Of the 6 cases studied, 3 showed what seemed to be a response to irradiation. Three cases showed no changes due to irradiation.

TABLE XII

No.	Case	Response	No. of Series	Average Time between Series	Average Tumor Dose per Series	Total Time under Treatment	Total Tumor Dose	Time Specimen Taken after Last Treatment
1	H. B.		1		2,365 r	29 days	2,365 r	3 mo.
2	R. A.		4	3.5 mo.	740 r	11 mo.	2,958 r	9 mo.
3	E. O.		5	3.6 mo.	1,430 r	19 mo.	7,120 r	12 mo.
4	H. D.		1		2,061 r	25 days	2,061 r	1.3 mo.
5	E. J.	—	2	1.5 mo.	577 r	2.3 mo.	1,155 r	2.5 mo.
6	C. W.	—	1		1,460 r	17 days	1,460 r	3 mo.
7	A. J. R.	—	1		567 r	5 days	567 r	1 day

In comparison with the medulloblastomas, the cells of the glioblastomas apparently show a greater degree of resistance to roentgen irradiation. Wide variations in the cytological appearance may be present, yet as a group there seems to be some correlation between the quantity of radiation delivered and the demonstrable destructive effect of irradiation. In these tumors it is essential to deliver a "skin tolerance" dose of radiation through as many as four or five portals. While the time interval between series should be as short as is consistent with safety to the skin and overlying structures, it may be longer than that advisable in the medulloblastomas.

The astrocytoma is a benign tumor composed for the most part of adult cells. Theoretically, it would respond poorly, if at all, to irradiation. This is true of 3 of our cases. The other 3 cases showed what seemed to be definite responses to irradiation.

An adequately treated case with a good histologic response is seen in the following instance:

CASE A. H. (Surg. Nos. 12330, 20171). *A large astrocytoma of the left frontoparietal region. Intensive irradiation. Eleven courses. Definite changes in the tumor following radiation therapy.*

History. The patient, male, aged thirty-six, was admitted to the University Hospital for

the first time on November 17, 1927, in the care of Dr. C. H. Frazier. He had been struck by a baseball in 1917 and was unconscious for ten minutes. In 1920, ten years before admission, he first noticed paresthesia in the right side of the neck and shoulder. These sensations occurred in attacks lasting one to two minutes, occurring every two to three weeks. Shortly after this he developed intermittent twitches of the right shoulder. In 1924, six years before admission, he developed attacks of numbness of the right arm associated with weakness of this member. About eighteen months before admission he had an attack of numbness involving the right side of the face and neck, and continued to have attacks of this nature from time to time. For about four years he had had convulsive seizures involving the right side.

Neurological examination at this time revealed anesthesia to touch and pin-prick of the right face, arm, and shoulder. There was a slight right central facial weakness, impairment of hearing on the right side, and generally hyperactive tendon reflexes. The spinal fluid pressure was 150 mm. of water. There was no papilledema. The blood and spinal fluid serology was negative.

Operation was performed on November 23, 1927, by Dr. C. H. Frazier. A left-sided craniotomy was performed. An infiltrating tumor was found high up in the left precentral area.

The following roentgen treatments were given:

1st series: Dec. 19, 1927 to Jan. 11, 1928, tumor dose 856 r, period 23 days, λ effective 0.17Å.
2nd series: Feb. 27 to March 23, 1928, tumor dose 1,579 r, period 24 days, λ effective 0.17Å.
3rd series: Aug. 13 to Aug. 22, 1928, tumor dose 1,579 r, period 9 days, λ effective 0.17Å.
4th series: Oct. 17 to Nov. 1, 1928, tumor dose 1,579 r, period 15 days, λ effective 0.17Å.
5th series: May 13 to June 1, 1928, tumor dose 1,579 r, period 19 days, λ effective 0.17Å.
6th series: Nov. 19 to Nov. 29, 1929, tumor dose 856 r, period 10 days, λ effective 0.17Å.
7th series: Apr. 28 to May 16, 1930, tumor dose 1,579 r, period 10 days, λ effective 0.17Å.

Second Admission, October 17, 1930. During the two year interim of his first and second admission he received seven courses of radiation therapy. Following each of these he felt distinctly improved and was able to carry on a fairly normal life. About ten days before his second admission he again developed a clonic convulsion of the right side. He developed more convulsions. Operation was not advised on this second admission but radium was suggested in August, 1930. He was given radiation therapy and discharged.

Radium treatment August to December, 1930, 25,776 mg-hr. at 4 cm. distance, filtration 0.5 mm. Ag and 3 mm. Pb.

Third Admission, April 6, 1931. In January, 1931, about four years after his operation, he became gradually weak in his entire right side. He developed aphasia and intense headaches. Examination at this time revealed a right flaccid hemiplegia, right-sided astereognosis, motor aphasia, hyperactive reflexes on the right side, and emotional instability. There was 4D of choking in each eye. The spinal fluid pressure was 180 mm. of water.

Second Operation, April 8, 1931. Dr. F. C. Grant re-elevated the left temporoparietal bone flap and removed most of an infiltrating tumor at the top of the left precentral gyrus. He improved following operation and was given further radiation treatment:

8th series: June 18 to July 3, 1931, tumor dose 856 r, period 16 days, λ effective 0.17 Å.
9th series: Aug. 27 to Sept. 10, 1931, tumor dose 1,200 r, period 14 days, λ effective 0.17 Å.
10th series: Oct. 29 to Nov. 13, 1931, tumor dose 2,075 r, period 15 days, λ effective 0.17 Å.
11th series: Jan. 4 to Jan. 15, 1932, tumor dose 1,510 r, period 11 days, λ effective 0.17 Å.
12th series: March 1 to March 9, 1932, tumor dose 1,442 r, period 8 days, λ effective 0.17 Å.
13th series: May 23 to June 3, 1932, tumor dose 865 r, period 11 days, λ effective 0.17 Å.

Fourth Admission. Despite his second operation he went gradually downhill, became very cachectic, developed decubitus ulcers, and died in October, 1932.

Necropsy revealed a large tumor infiltrating the left cerebral hemisphere. This seemed to begin in first frontal gyrus, on the left side and extended posteriorly to the superior parietal lobule. It invaded the left paracentral lobule and the precuneus region. It invaded also the middle third of the body of the corpus callosum. The tumor was firmly adherent to the dura. Its cut surface was necrotic, and it had a coarse fibrotic appearance.

Histological Studies:

Pre-irradiaion Specimen (November 23, 1927). A biopsy from the first operation in 1927 was diagnosed medulloblastoma in another

laboratory. A review of this specimen showed it to be an astrocytoma. The cells were arranged in irregular columns and lay in a dense network of fine neuroglia fibrillae. It was extremely vascular. The cells were typical astrocytes.

Post-irradiation Specimen. The first specimen available for study was in 1931. This was taken four months following the last radium treatment. This showed an orderly arrangement of the cells in columns. The nuclei were uniformly round and the cytoplasm was either not visible or was seen as a very thin bit of tissue around the nucleus. Vessels were numerous and showed no changes. There was little stroma except around the vessels. The tumor appeared to be a typical astrocytoma. In a few areas the tumor cells appeared to be somewhat disturbed in arrangement, but this was not a very common finding.

The specimen obtained at autopsy in 1932, four months after the last roentgen treatment, was definitely different: (1) the orderly arrangement of the cells, noted in the previous specimen, was entirely absent. The cells were strewn about in lobules or in disorderly groups quite in contrast with the previous specimen; (2) there was widespread pyknosis of the nuclei in most parts of the tumor. Other parts contained cells which were normal in appearance; (3) the fibrous tissue content of the tumor was markedly increased in this specimen. Everywhere were large areas of fibrous tissue which filled the tumor and displaced most of the cellular portion of the tissue; (4) an increase in the delicate reticular tissue in the tumor.

In this case the post-irradiation specimen revealed a marked disturbance of the orderly structure of the tumor so that the original tumor structure was hardly discernible. Furthermore, there was a widespread pyknosis of the nuclei and a marked increase in the collagenous stroma.

Another case which seemed to show definite changes after irradiation is seen in the following instance:

Case E. L. (Surg. Nos. 16728, 16889, 18001). *Astrocytoma of left temporal lobe. Mild changes after three courses of irradiation.*

History. The patient, a male, aged fifty-eight, entered the University Hospital August 10, 1929. For two years he had had mild headaches and attacks of indigestion. These had been much worse for a month before entrance. During this time he developed inability to talk and to understand, as well as a progressive weakness of the right side of the body. For three weeks he had been helpless, and was incontinent.

Neurological examination revealed bilateral choked disc of 3D in each eye. There was a right hemiplegia, a motor and sensory aphasia, and fixed pupils with absent patellar and corneal reflexes. A diagnosis of left temporal lobe tumor was made.

Operation. On August 14, 1929, Dr. Frazier threw back a left temporoparietal bone flap. An infiltrating tumor was found in the left temporal lobe and most of it removed. The patient made a good recovery and was discharged August 27, 1929.

Second Admission. He returned to the hospital on September 10, 1929, for irradiation of the tumor. There had been marked improvement since discharge. He was able to walk with a cane, the headache had disappeared, and he was less somnolent. He was discharged after the irradiation.

1st series: Sept. 10 to Sept. 16, 1929, tumor dose 1,548 r, period 6 days, λ effective 0.17Å.
2nd series: Nov. 11 to Nov. 22, 1929, tumor dose 1,548 r, period 11 days, λ effective 0.17Å.

Third Admission. He was again admitted January 27, 1930, having received one additional course of irradiation in the meantime. In January, 1930, he had a recurrence of his symptoms and again developed complete aphasia.

Second Operation. On February 20, 1930, Dr. Frazier again operated and removed what remained of the tumor. The patient died the following day.

Necropsy revealed a tumor of the left temporal lobe, invading the basal ganglia on the left side.

Histological Studies:

Pre-irradiation Specimen (August, 1929). The tumor is quite cellular, the cells being packed into rather a solid structure. Vessels are numerous. There is little fibrous stroma and only a moderate amount of intercellular fibrils. The cells have elongated, vesicular nuclei and a roomy cytoplasm.

Post-irradiation Specimen (three months after last treatment of the second series). This specimen differed definitely from the first. The cells are arranged in columns. Many of them

are in small groups and acini. Cords of cells are frequently seen. Fine strands of connective tissue are seen among the cells. There is much intercellular tissue composed of glia fibrils which penetrate everywhere among the cells. Adult astrocytes are seen in great abundance in this specimen but were not found in the first specimen.

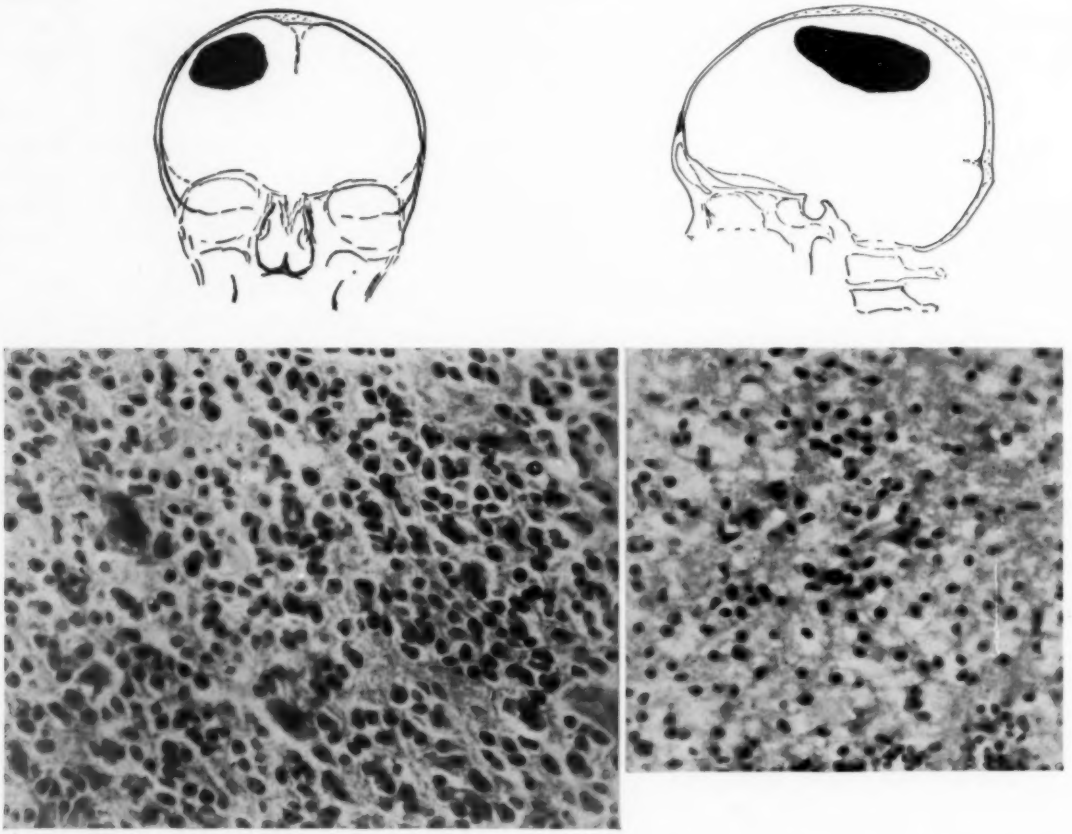


Fig. 10. Case A. H. Astrocytoma of left frontoparietal region. Tumor dose adequate. Series doses inadequate. Interval between series too long. Marked histological changes. *Irradiation data:* Thirteen series, period four and a half years, tumor dose 15,580 r, λ effective 0.17 Å. Radium—period one month, 25,776 mg-hr., three portals, distance 4 cm., filter 0.5 mm. Ag plus 3 mm. Pb. *Pathology:* The tumor is less cellular and has more neuroglia fibrils after irradiation (lower right).

Here the post-irradiation change was different from that of the preceding case. The original tumor was composed of cells closely packed, with elongated nuclei, with numerous vessels and little stroma. After irradiation the structure was definitely that of a mature astrocytoma with many immature astroblasts. Areas of necrosis were numerous, adult astrocytes were present everywhere, and there was a marked increase in the amount of glial fibrils everywhere in the specimen. We see here, therefore, a tumor which was originally composed largely of immature cells, probably astroblasts, which under the influence of irradiation developed into mature astrocytes. The same process might have occurred without irradiation but in our experience such a metamorphosis is quite unusual in the growth of these tumors.

Less pronounced effects are seen in the following case:

Case R. L. (Surg. No. 18110). *Astrocytoma with three courses of moderately intensive irradiation. Moderate changes in the tumor.*

History. The patient, a male, aged seventeen, entered the University Hospital February 10, 1930. He had been well until a year before when he developed headaches which were continuous and persistent. On a few occasions he developed transitory blindness.

Neurological examination revealed bilateral choked disc. There was disturbance in gait, but no other visible signs.

Operation. On February 17, 1930, Dr. Frazier performed a suboccipital craniectomy. A left cerebellar tumor was exposed. Recovery was uneventful.

series: April 12 to May 10, 1932, tumor dose 1,542 r, period 28 days, λ effective 0.17 Å) which improved his condition for a time but was again followed by headache and vomiting. Neurological studies at this time showed a marked dyssynergic gait, unsteady station, nystagmus, and 4D choking in each eye.

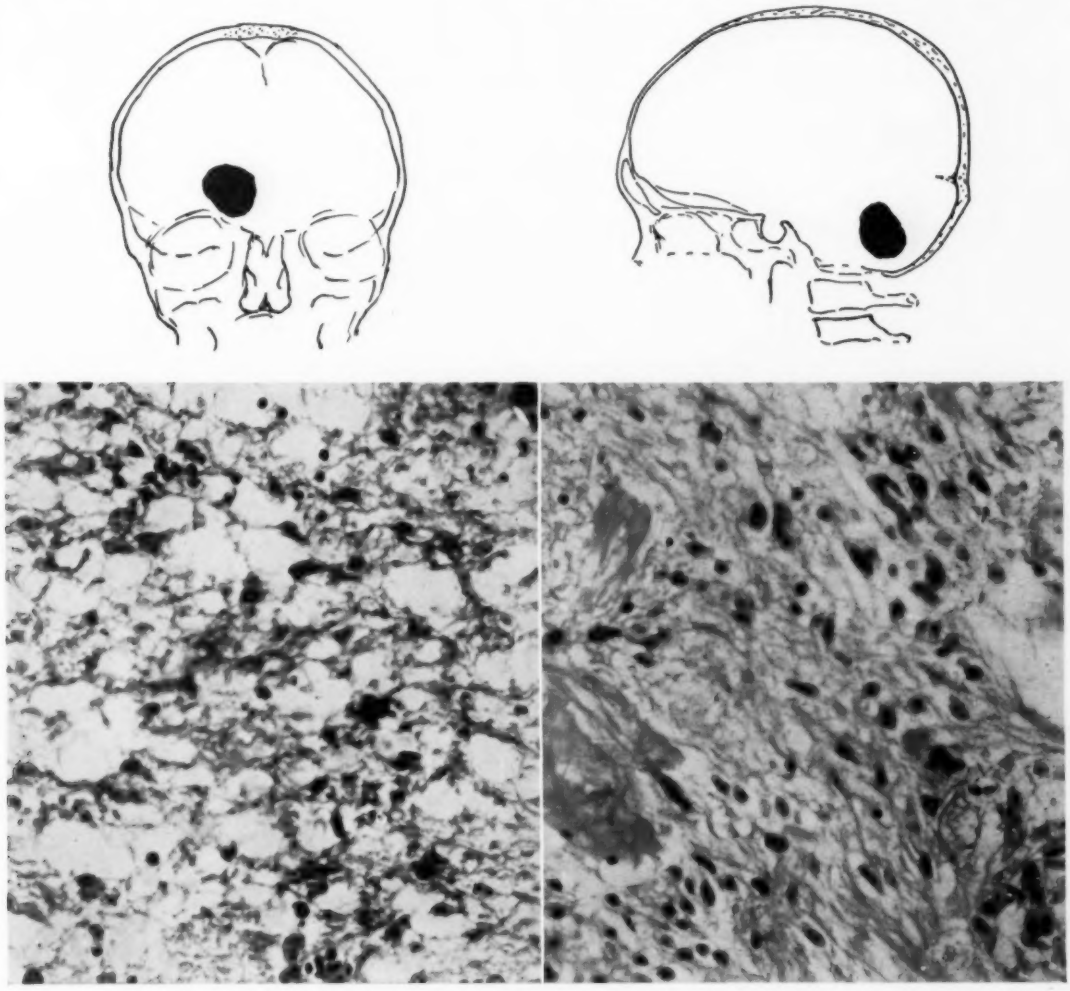


Fig. 11. Case R. L. Astrocytoma of left cerebellar hemisphere. Tumor dose adequate. Series doses inadequate. Series interval too long. Moderate histological effects. *Irradiation data:* Three series, period two years six weeks, tumor dose 3,739 r, λ effective 0.17 Å. *Pathology:* The increase in neuroglia fibrils after irradiation (lower right) is quite apparent.

1st series: March 22 to April 23, 1930, tumor dose, 1,292 r, period 32 days, λ effective 0.17 Å.
2nd series: June 30 to July 14, 1930, tumor dose 812 r, period 14 days, λ effective 0.17 Å.

Following operation he received two courses of irradiation as above. He felt well for a time and again developed headache and vomiting. He was given another course of irradiation (3rd

Second Operation. On June 29, 1932, Dr. Frazier again operated and removed most of the tumor in the left cerebellar hemisphere. Recovery was uneventful.

He remained well until six months before entrance when headaches and vomiting recurred. This was followed gradually by unsteadiness in gait.

Third Operation. On September 29, 1934, Dr. Frazier again removed what appeared to be all of the tumor. The patient made a good recovery and is still alive.

Histological Studies:

First Post-irradiation Specimen (June 1932). This is a typical astrocytoma.

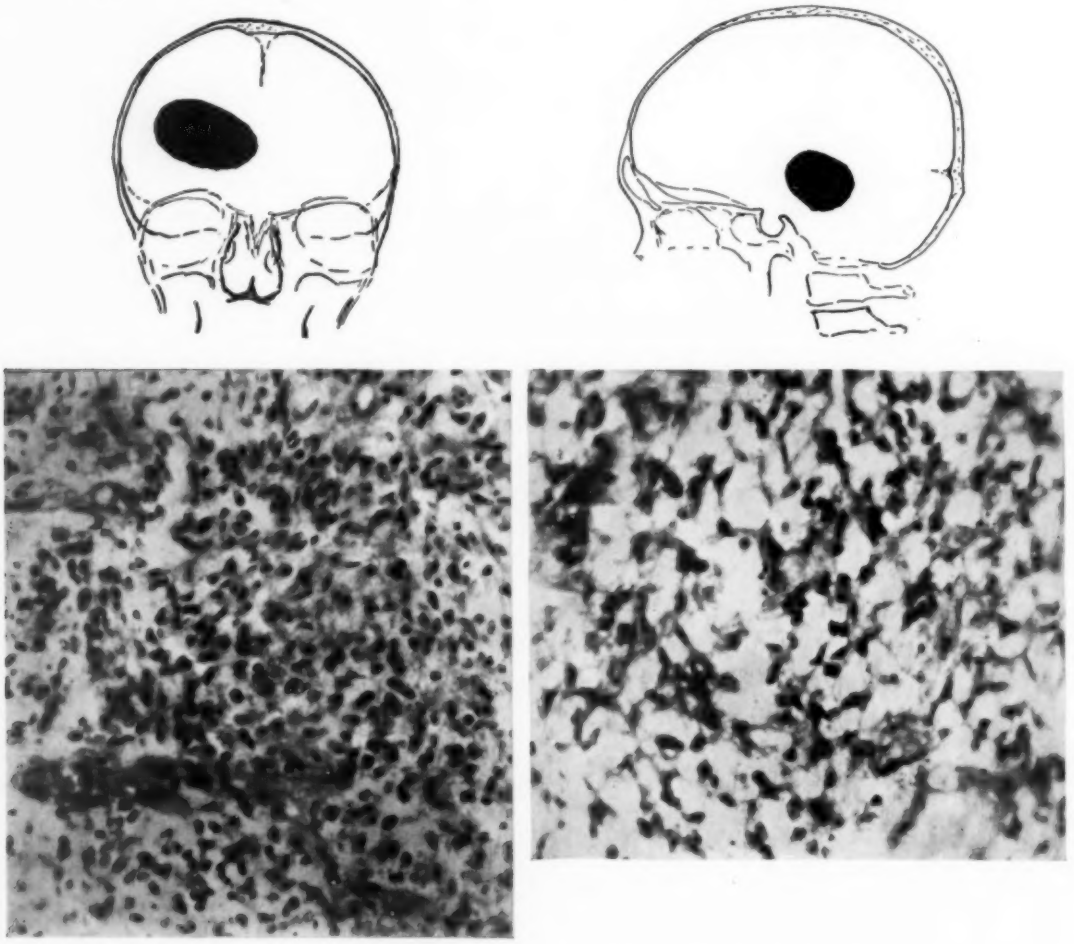


FIG. 12. Case E. L. Astrocytoma of left temporal lobe. Tumor dose adequate. Series doses inadequate. Series interval correct. Marked histological effects. *Irradiation data:* Three series, period five months, tumor dose 3,096 r, λ effective 0.17 Å. *Pathology:* There is a great increase in the interstitial neuroglia fibrils after irradiation (lower right).

Second Post-irradiation Specimen (Sept. 1934, twenty-eight months after last treatment). This is quite different from the first post-irradiation specimen: (1) the vessels are much more numerous; many of them are hyalinized; others show a proliferation of the vessel walls. These changes were not present in the first post-irradiation specimen; (2) the fibrous stroma is definitely more abundant in this specimen; (3) there are many multinucleated cells as compared with the first post-irradiation specimen which had only scattered cells of this nature.

Here, too, post-irradiation effects seemed to be definite. There were many more multinucleated cells in the post-irradiation specimen. Fibrous stroma was much more abundant, penetrating everywhere through the tumor in long prolongations. The blood vessels were more numerous and often hyalinized, a change which we have seen not infrequently in other tumors after irradiation.

Summary of Histological Findings. Of the 6 astrocytomas studied, 3 showed a good response to irradiation. The response of the cells in 2 of these cases was quite

striking. Under the influence of irradiation the cells developed into more mature forms. In the pre-irradiation specimens they were immature in type, but after irradiation the cells were seen as true astrocytes. They had not been present in the pre-irradiation specimen. Whether the cells matured because of the irradiation is hard to say. Certainly under the influence of irradiation the cells of these two tumors developed from astroblasts to astrocytes. In one of these tumors also there was a great increase in the number of multinucleated cells after irradiation. In all these tumors which responded to irradiation, there was an increase in the fibrous stroma and in the deposit of neuroglia fibrils among the cells (Figs. 10, 11 and 12). Few changes were noted in the vessels.

TABLE XIV

INTERVAL BETWEEN TREATMENT AND POST-IRRADIATION BIOPSY OR NECROPSY IN THE ASTROCYTOMA GROUP

Case	Interval between Treatment and Biopsy or Necropsy	
	First treatment to biopsy	Last treatment to biopsy
A. H.	40 mo. to biopsy 58 mo. to necropsy	10 mo. to necropsy
M. N.	29 days	22 days
E. L.	5 mo.	3 mo.
R. L.	52 mo.	28 mo.
H. K.	7 mo.	2 mo.
F. L.	35 mo.	32 mo.

TABLE XV

INTERVAL BETWEEN SERIES OF THE ASTROCYTOMA GROUP

Case	No. Series	Interval between Series				
		1st to 2nd	2nd to 3rd	3rd to 4th	4th to 5th	5th to 6th
A. H.	10	9 wk.	5½ mo.	8 wk.	7 mo.	11 mo. 5½ mo. 14 mo. 2 mo. 2 mo.
M. N.	1					
E. L.	3	4 wk.	4 mo.			
R. L.	3	3 mo.	22 mo.			
F. L.	2	11 wk.				
H. K.	3	8 wk.	10 wk.			

The astrocytomas have been regarded in the past as radioresistant tumors and irradiation of this group has been more or less discouraged. This appears to be true for the most part, since 3 of our 6 cases did not respond to irradiation. Of these 3, however, only one was well treated, so that it is not certain whether with proper therapy they too might not have shown some change after irradiation. In any event, our experience indicates that some astrocytomas are radiosensitive, at least in some degree. This appears to be true of the tumors in this group which are not wholly matured, for in 2 instances of this type our histological studies revealed a definite maturation of the cells while the tumor was under treatment. This is certainly an indication of a tendency for these tumors to assume a more benign appearance under the influence of irradiation.

Astrocytomas, therefore, may be radiosensitive to some degree and irradiation appears to be indicated in this group of tumors.

Analysis of Irradiation Data of the Astrocytoma Group. Each of the cases which showed histological response to irradiation received a total tumor dose greater than 3,000 r. All of those which showed no demonstrable effect received a total tumor

dose of less than 2,600 r. It is also worthy of note that each of the patients in whom the effect of irradiation was noticeable received at least two series of moderately intensive roentgen irradiation, while none of those showing no response received such intensive series. One case (A.H.) is of unusual interest. This patient, we feel sure, showed clinical improvement following irradiation, and probably roentgen therapy was responsible for the prolongation of life. This patient received a total of 15,500 r plus 25,750 mg-hr. of radium over a period of four and a half years. Most of the series given consisted of 800 r (measured in air) delivered through two or three portals. We now believe that this was very likely an inadequate form of therapy. Further support of this theory is obtained from the analysis of the irradiation of Case E.L. This case showed the same quantitative degree of response as Case A.H., yet the former received only two series (five months' period) consisting of 1,600 r through each of two portals. In those cases which showed no irradiation effect the dose in air was never more than 800 r through any one portal. We believe that doses of 2,000 to 2,400 r can safely be given in most cases through each of several portals.

The results in this group of tumors show a degree of radiosensitivity which would warrant further carefully planned roentgen therapy. It is our opinion that this group of tumors should have a much larger tumor dose at each series than any which we have given (see Table XVI).

EPENDYMOMAS

Two ependymomas were studied both before and after irradiation. Both of these were definitely affected by irradiation. Both cases were adequately treated from the radiological viewpoint.

CASE M. D. (Surg. Nos. 13193 and 19368). *A temporal ependymoma successfully removed. Four courses of irradiation after first removal. Definite changes in irradiated tumor.*

History. The patient, a woman, aged thirty-one, entered the University Hospital April 5, 1928, in the care of Dr. C. H. Frazier. She had had a discharging right ear for many years. Except for this she was well until six weeks before entrance when she developed severe headache. This became much more severe three weeks before entrance. She also had a constant buzzing in both ears, projectile vomiting, and pain in the head and left shoulder. She developed blurring vision before entrance.

Neurological examination revealed 4D of swelling in the left eye and 3D in the right. The mental responses were somewhat delayed. There was some impairment of position sense in the left hand and foot. There was a suggestive left central facial weakness, a hyperactive left patellar reflex, and a suggestive left Babinski. Hearing was bilaterally impaired. The visual fields were normal except for a temporal cut in the left field.

The roentgen examination of the skull was negative. The spinal fluid pressure was 20 mm. Hg.

Craniotomy was performed on April 10, 1928, by Dr. C. H. Frazier and an encapsulated glioma removed in its entirety. Two weeks later she had a moderate degree of astereognosis of the left hand, and impairment of position sense. Otherwise she made a very good recovery from operation.

The following roentgen treatments were given:

1st series: June 4 to June 14, 1928, tumor dose 1,445 r, period 10 days, λ effective 0.17Å.
2nd series: Aug. 14 to 23, 1928, tumor dose 1,445 r, period 9 days, λ effective 0.17Å.
3rd series: Nov. 5 to 21, 1928, tumor dose 1,445 r, period 16 days, λ effective 0.17Å.
4th series: July 10 to 18, 1929, tumor dose 1,445 r, period 8 days, λ effective 0.17Å.

Second Admission, July 7, 1930. Following operation the patient did very well until May, 1930, when she complained of trembling spells and numbness in the left hand and arm. These became progressively weak and necessitated her entrance into hospital. Neurological examination at this time showed a left hemiparesis, left-sided astereognosis and dyssynergia, and decreased pain, heat and cold sensations over the entire left side of the body. There was now 1.5D choking in the left eye and 2D in the right. Both temporal fields showed severe cuts.

Second Operation, July 12, 1930. The original bone flap was reflected by Dr. C. H. Frazier and a recurrent tumor was removed from the

right temporal region. Recovery was uneventful.

Histological Studies:

Pre-irradiation Specimen (April 10, 1928). This specimen, removed two years before the post-irradiation specimen, was a typical ependymoma. The cells were arranged in streams or around the vessels, with the characteristic perivascular arrangement of the cells. There was only a slight degree of stroma in the tumor, chiefly around the vessels.

Post-irradiation Specimen (July 12, 1930, one year following the last roentgen treatment). There was a definite difference between the specimens before and after irradiation. In the pre-irradiation specimen the cells were arranged in solid masses. This was not apparent after irradiation. The following changes were noted: (1) The consistency of the tumor was changed. There were more areas of necrosis. The cells were arranged in irregular, loosely arranged groups as compared with a solid mass of tumor tissue before operation. (2) The cells in the tumor revealed a remarkable change after irradiation. Before irradiation they had a more or less uniform appearance with oval or round nuclei and a bipolar type of cytoplasm. Following irradiation there was a marked metamorphosis. The cells showed a severe polymorphism. Hardly two cells were alike. They now had round hyperchromatic nuclei with a round granular cytoplasm. There were extremely large cells and also multinucleated giant cells which could not be found in the pre-irradiation specimen. Many of the cells had a necrotic appearance. The significance of this cell change is not clear but it is definite. The post-irradiation specimen has a more benign appearance from the cellular standpoint. (3) The vessels in the post-irradiation specimen are thicker and their walls more proliferated. (4) There are large areas of fatty necrosis of cells in the post-irradiation specimen, but not in the tissue before irradiation.

This case showed definite changes in the post-irradiation specimen. The histological appearance of the second specimen was so strikingly different from the pre-irradiation specimen that they hardly looked like the same tumor.

Table XVI

No.	Case	Response	No. of Series	Average Time between Series	Average Tumor Dose per Series (r)	Total Time under Treatment	Total Tumor Dose (r)	Time Specimen Taken after Last Treatment
1	A. H.		13	4 mo.	1,198	4.5 yr.	15,580 + radium	10 mo.
2	E. L.		2	2 mo.	1,548	5 mo.	3,096	3 mo.
3	R. L.		3	8 mo.	1,246	25 mo.	3,739	28 mo.
4	M. N.	—	1		600	8 days	600	22 days
5	H. K.	—	3	1.2 mo.	861	5 mo.	2,585	2 mo.
6	F. L.	—	2	1.5 mo.	722	3 mo.	1,445	?

Another instance of good irradiation effects in this type of glioma is found in the following case:

Case C. R. (Surg. Nos. 9361, 12327, 14095, 15352, 16344, 16914). *Ependymoma with four courses of irradiation. Definite changes in the tumor attributable to irradiation.*

History. The patient, a girl, aged nineteen, entered the University Hospital in June, 1926. Two years ago she had been struck in the left temple by a baseball. In December, 1925, about a year before entrance, she suddenly developed bilateral frontal and temporal headache with pain in the back of the neck. This was accompanied by vomiting. These symptoms persisted. She developed diplopia eight months before entrance, with internal strabismus of the right eye. On admission the patient still complained of headache but there was no diplopia or squint.

Neurological examination revealed 5D choking in each eye. There was a quadrantic temporal defect in the left visual field. The spinal fluid pressure was 26 mm. Hg. She had visual hallucinations, and a suggestive weakness of the right arm. A right temporal lobe lesion was diagnosed.

Operation. On June 12, 1926, Dr. Frazier evacuated a gliomatous cyst in the left temporal lobe. Convalescence was uneventful.

Second Admission. The patient was readmitted on October 13, 1926, and the cyst again evacuated because she had developed headaches in the meantime and had lost much vision from secondary optic atrophy.

1st series: Nov. 4 to 15, 1926, tumor dose 410 r, period 11 days, λ effective 0.17 Å.

Second Operation. On January 17, 1927, Dr. Grant reflected a left temporoparietal bone flap and found a large tumor in the wall of the ventricle. A large part of the tumor was removed.

2nd series: Dec. 16, 1927 to Jan. 4, 1928, tumor dose 1,340 r, period 19 days, λ effective 0.17 Å.

Third Admission. A course of irradiation was given but no operation was attempted. She had developed Jacksonian fits of the right side in the meantime but they were not very frequent.

Fourth Admission. The convulsive seizures recurred about every two weeks but there had not been an attack for about two months before her admission on June 3, 1928. No irradiation was given at this time.

Fifth Admission. Because of the persistent convulsions which were mainly right-sided, it was decided to re-operate. Her neurological condition at this time showed subsidiary choked disc with secondary atrophy, and dysmetria and weakness of the right arm and leg.

Third Operation. On February 15, 1929, Dr. Grant re-elevated the old skin flap and at this time removed a large tumor in toto. After recovery from the operation a course of irradiation was given.

3rd series: March 11 to 21, 1929, tumor dose 1,200 r, period 9 days, λ effective 0.17 Å.

Sixth Admission. The patient returned June 17, 1929, for irradiation of the tumor.

4th series: June 17 to 26, 1929, tumor dose 1,340 r, period 9 days, λ effective 0.17 Å.

She had had almost daily attacks since her last admission and was now complaining of tingling in the right side of the mouth, inability to speak, and jerking movement of the tongue. She improved slightly after irradiation.

Seventh Admission. The patient was readmitted in September 13, 1929, because of convulsions. These had been frequent since her last operation.

Fourth Operation. On October 4, 1929, Dr Frazier again removed a large tumor mass from the left temporal region. She made a good recovery from this operation and survived until February 5, 1930, when she died.

Histological Studies:

First Post-irradiation Specimen (January, 1927). This specimen was taken two months after a single series of irradiation. There were no effects attributable to the irradiation. The tumor is very cellular. There is a tendency for the cells to be arranged around vessels with the cell bodies settled against the vessel wall. The nuclei are round or oval and surrounded by a roomy polygonal cytoplasm which has a heavy cytoplasmic membrane. Mitoses are not very numerous. Stroma is seen as fine strands of collagen penetrating into the tumor.

TABLE XVII

INTERVAL BETWEEN TREATMENT AND POST-IRRADIATION BIOPSY OR NECROPSY IN THE EPENDYMOMA GROUP

Case	Interval between Treatment and Biopsy or Necropsy	
	First treatment to biopsy	Last treatment to biopsy
C. R.	2 mo.	12 mo.
M. D.	25 mo.	12 mo.

TABLE XVIII

INTERVAL BETWEEN SERIES OF THE EPENDYMOMA GROUP

Case	No. Series	Interval between Series		
		1st to 2nd	2nd to 3rd	3rd to 4th
M. D.	2	10 wk.		
C. R.	4	13 mo.	15 mo.	3 mo.

Second Post-irradiation Specimen (two months and twelve months). These specimens differ quite markedly from those before irradiation: (1) There is much more necrosis, but this may be due to the manipulation at operation with consequent interference with blood supply. The first specimens show no necrosis, the later ones show a good deal. (2) There is also much more fibrosis in this specimen. It appears to radiate out from the vessel walls into all parts of the tumor. There are also many more glia fibrils among the tumor cells.

Specific stains show a large number of fibrils everywhere in the tissue. (3) There are extensive changes in the vessels. These are not seen in the first post-irradiation specimen. These changes are seen in the adventitial proliferation which is present in almost all the vessels.

In this case there was much more necrosis and a much richer fibrous stroma following irradiation. The cells stained less intensely. The vessels showed a definite tendency toward adventitial proliferation. Some of these changes might readily be attributed to the effects of operative interference since there had been three craniotomies.

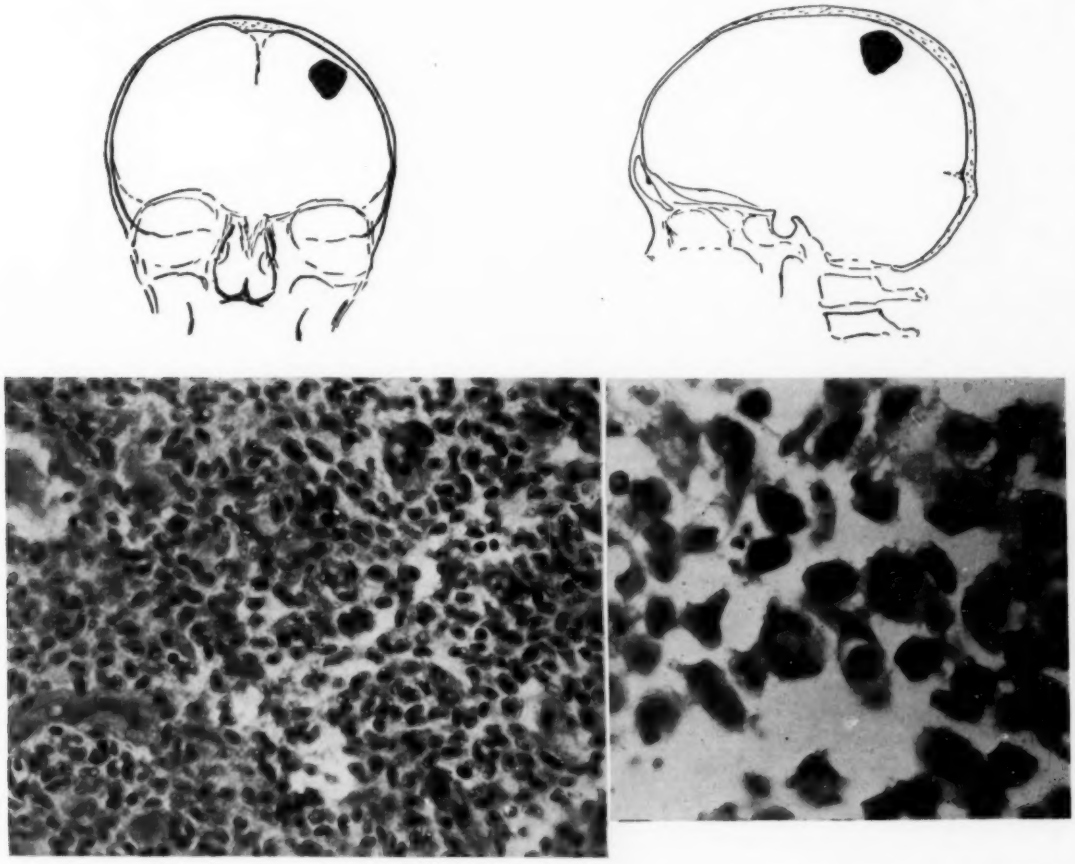


Fig. 13. Case M. D. Ependymoma of the right parietal lobe. Tumor dose adequate. Series doses inadequate. Series interval correct. Marked histological effects. *Irradiation data:* Four series, period one year six weeks, tumor dose 5,779 r, λ effective 0.17 Å. *Pathology:* The tissue before irradiation (lower left) shows a compact cellular structure. Note the extensive necrosis and the large swollen cells after irradiation (lower right).

Summary of Histological Findings. Both our cases of ependymoma showed marked changes after irradiation. These changes were of two types involving the cells and stroma. In one case particularly there was a marked metamorphosis of the cells. In the pre-irradiation specimen they were of an immature type. In the post-irradiation specimen they were of a mature type, with a totally different structure, and with a markedly different appearance (Fig. 13). In the other case, there were changes in the cells of a similar nature but they were not nearly as pronounced as in the first case (Fig. 14). In both cases also, there was an increase in fibrous stroma, thickening of the vessels with fatty degeneration in one case, and increase in the amount of necrosis after irradiation.

Irradiation appears to have a very definite effect on ependymomas. Both our cases assumed a more benign character under the influence of irradiation. We received a total of 5,700 r. Here again, however, the dose given at each series was limited to 800 r (measured in air) through any one portal. We now believe that his-

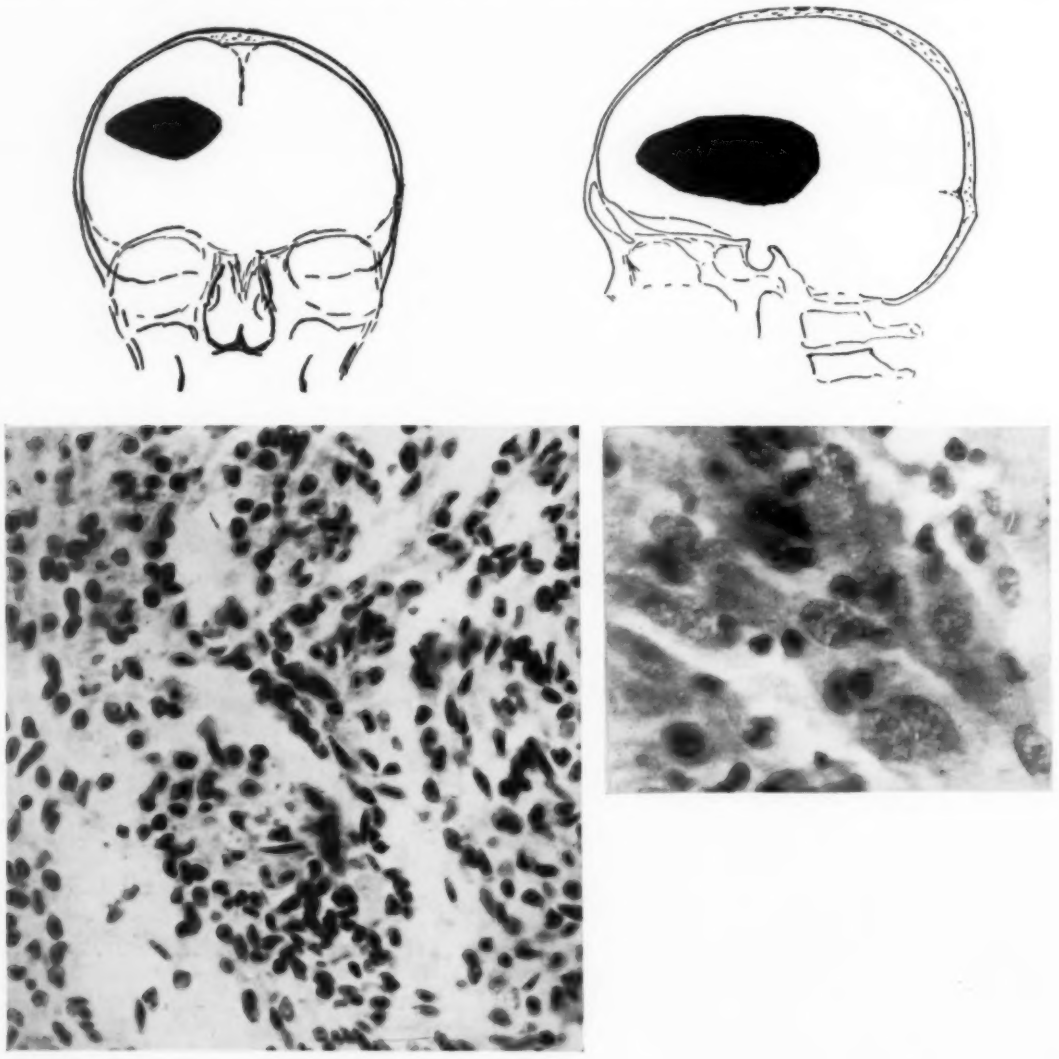


FIG. 14. Case C. R. Ependymoma of left temporoparietal lobe. Tumor dose adequate. Series doses inadequate. Series interval too long. *Irradiation data:* Four series, period two years seven months, tumor dose 4,469 r, λ effective 0.17 Å. *Pathology:* Note the great difference in the cells after irradiation. The cells are larger, more mature, and the tumor resembles more a mature ependymoma than the pre-irradiation tumor (lower left).

gard irradiation as a good adjunct to surgery in this type of tumor.

Analysis of Irradiation Data in Ependymomas. Each of the 2 cases presented in this group received a tumor dose greater than 4,000 r. The most marked irradiation effects were noted in Case M.D., which retologically these two tumors showed marked effects, although radiologically they were inadequately treated. This is true particularly from the standpoint of quantity of radiation delivered in any one series. The possibility of improvement in our clinical results and histological

Table XIX

INTERVAL BETWEEN TREATMENT AND POST-IRRADIATION BIOPSY OR NECROPSY IN THE OLIGODENDROGLIOMA GROUP

Case	Interval between Treatment and Biopsy or Necropsy	
	First treatment to biopsy	Last treatment to biopsy
A. W.	13 mo.	7 days
B. G.	13 mo.	14 mo.
J. G.	23 mo.	13 mo.

Table XX

INTERVAL BETWEEN SERIES OF THE OLIGODENDROGLIOMA GROUP

Case	No. Series	Interval between Series		
		1st to 2nd	2nd to 3rd	3rd to 4th
A. W.	4	8 wk.	3 mo.	7½ mo.
T. G.	4	9 wk.	10 wk.	6 mo.
B. G.	1			

effects can be enhanced by the administration of a greater intensity of radiation over a given time.

OLIGODENDROGLIOMAS

Three tumors of this type were studied. In none of them was there any finding in the post-irradiation specimen which could be attributed to irradiation (Figs. 15 and

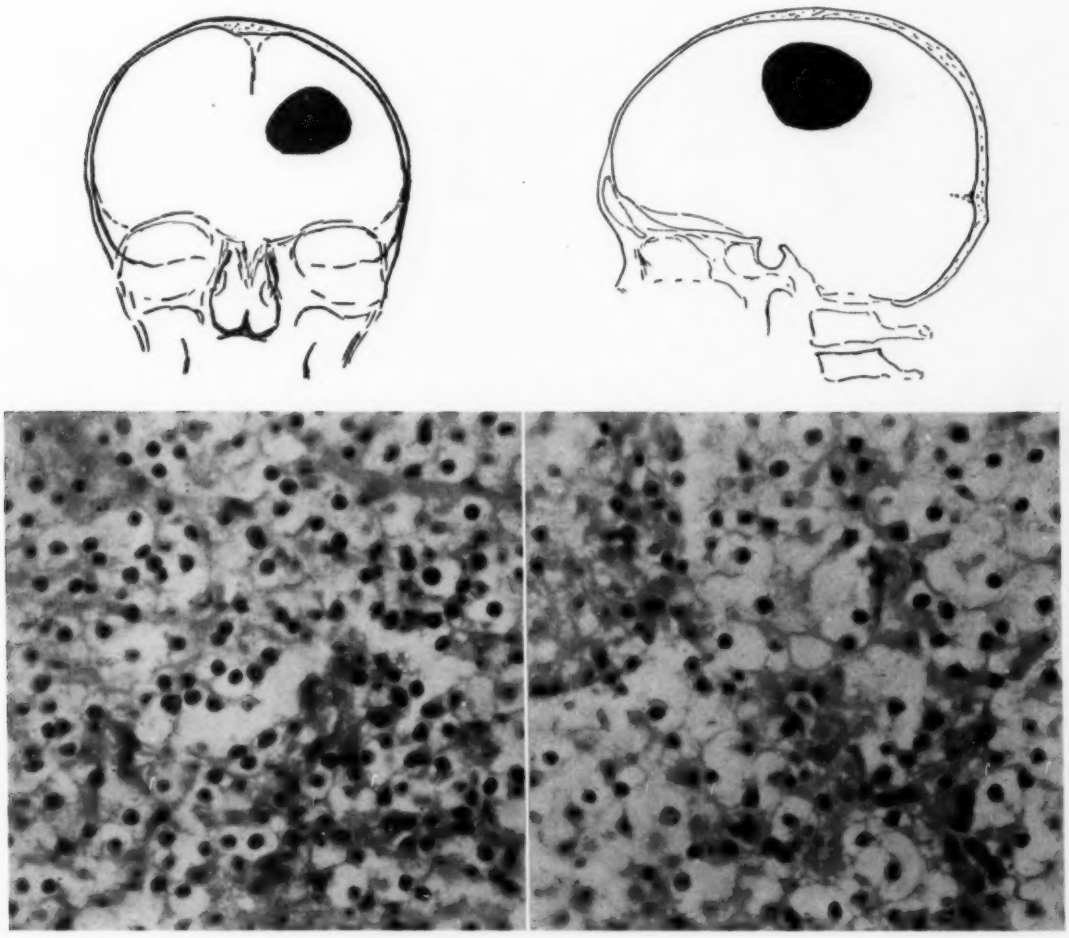


Fig. 15. Case J. G. Oligodendroglioma of right parietal lobe. Tumor dose adequate. Series doses inadequate. Series interval too long. No histological effects. *Irradiation data:* Four series, period ten months, tumor dose 2,680 r, λ effective 0.17 Å. *Pathology:* The irradiation has had no effect on the tumor structure.

16). These tumors are composed, for the most part, of adult cells which are quite resistant to irradiation. For all practical purposes they may be regarded as radioresistant tumors.

of the five groups which we have studied. If the evidence presented by this very small number of cases can be considered as applicable to these tumors as a group, then it is probably necessary to seek some form of therapy other than external irradiation.

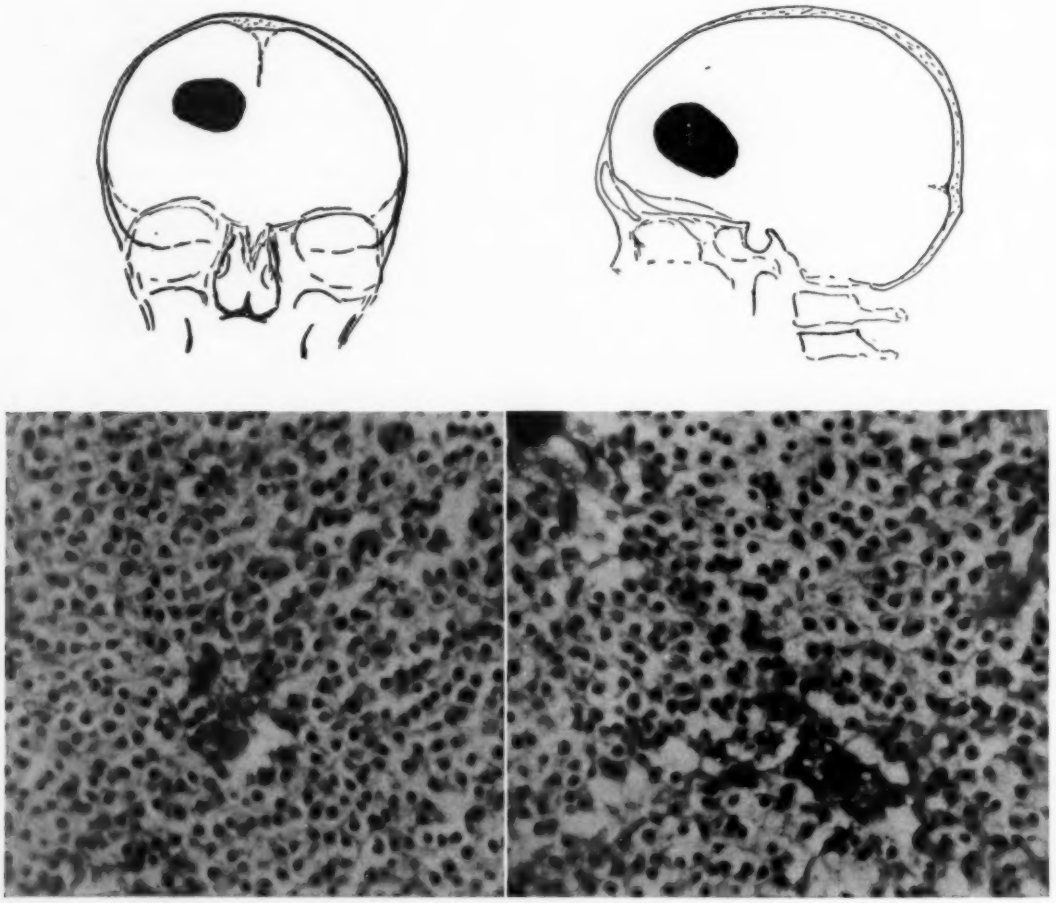


FIG. 16. Case A. W. Oligodendroglioma of left frontal lobe. Tumor dose adequate. Series doses inadequate. Series interval too long. No histological effects. *Irradiation data:* Four series, period thirteen months, tumor dose 5,366 r, λ effective 0.17 Å. *Pathology:* The irradiation has had no effect on the tumor structure.

Analysis of Irradition Data in the Oligodendrogliomas. The cases in this group which were considered as adequately treated received varying tumor doses from 1,084 to 6,400 r. While none of the cases was given extremely intensive series at brief intervals, the changes in the tumor cells following irradiation did not serve as an index of the quantity of energy delivered into the tumor. This group of tumors is apparently the most resistant

COMMENT ON IRRADIATION

At this time it seems advisable to review briefly our present knowledge of the biological effects of irradiation in general. "Radiosensitive" and "radioresistant" are words which are glibly used, yet we do not understand why some cells can be destroyed by a certain amount of roentgen

rays while other morphologically similar cells show no demonstrable changes. According to Packard,[6] the first biological effect of irradiation is a physical one. The quanta of radiation produce changes in the electronic fields of the atoms of protoplasm. This disturbance of electron balance produces changes in the hydrogen ion concentration, in the viscosity of the protoplasm, in the permeability of the cell membrane and in the respiratory rate. The secondary morphologic effects are demonstrable as clumping of the protoplasm, shrinking and agglutination of the chromosomes. Such changes as these may be reversible. If the intensity of radiation is great, some of the cells will show vacuolization of the cytoplasm and fragmentation of the mitochondria. When this occurs, the changes are said to be irreversible. These changes in the cell result in an alteration of the rate of cell division. From a study of tissue culture preparations, Strangeways and Hopwood[7] have shown that these cells which are in mitosis at the time of irradiation complete that process then remain quiescent, while those in a resting state are prevented from undergoing cell division. Fisher, Groot and Bachem[4] have shown that when the normal pancreas of dogs is exposed to 3 erythema doses of roentgen rays, some of the cells show varying degrees of destruction and death, while adjoining cells may present the picture of cell regeneration and reproduction. By using 4 erythema doses the regenerative changes were less marked, and after irradiation with 5 erythema doses no regeneration could be observed.

Clinical information and histological data obtained in the study of the more sensitive types of tumors of the kidney, bladder, breast, and even in the very sensitive lymphoblastomas, would indicate that unless the cells are injured beyond the irreversible stage regeneration does occur.

In the tumors of the medulloblastoma type, these biological principles are quite applicable. If one strives only for palliation it is probable that comparatively small doses of radiation delivered at frequent intervals of time would be adequate. If, however, we would hope to cure these patients we must use irradiation with the purpose of destroying the most resistant cells; with the intention of prohibiting mitosis, and producing the maximum amount of change in the stroma, which would, in turn, interfere with the nutrition of the cells. This may also be said of the glioblastoma multiforme group of tumors. In these cases the cells and stroma exhibit a more homogeneous reaction to irradiation but show a higher degree of resistance. In the astrocytoma group, in particular, the indications point toward much more intensive irradiation at each series. From the material presented, it would appear that similar comment may be made in regard to the ependymomas. The oligodendrogliomas studied have not shown any effect following irradiation and it is suggested that some form of therapy other than external irradiation be sought for in these cases.

We realize that irradiation, like surgery, has not solved the problem of therapy for the patient with a glioma. It is apparent that our present standards are only partially adequate. The evidence presented would indicate that many of those cases classified herein as receiving adequate treatment should subsequently be classified as inadequately treated.

SUMMARY AND CONCLUSIONS

1. Thirty gliomas were studied exhaustively before and after irradiation in order to determine the histological effects of irradiation for guidance in future treatment.

2. The cases were arbitrarily grouped as follows: inadequate treatment (less than 1,000 r), moderate treatment (1,000–2,000 r), adequate treatment (more than 2,000 r).

3. Of twelve medulloblastomas, five showed either a moderate or marked histological response to irradiation, five

showed a mild response, and two none at all. The histological effects were seen primarily in the cells, next in the connective tissue stroma, and least in the vessels.

4. The medulloblastomas are radiosensitive. Our data indicate that they should be treated at brief intervals of not more than six weeks between any two series. Each series should be delivered through a maximum number of skin portals. Approximately 2,000 r (measured in air) can be safely delivered to each portal.

5. Of seven cases of glioblastoma multiforme, only four showed mild response to irradiation. These were indefinite. They were exhibited in an increase in pseudomitoses and giant cells, and a slightly increased fibrosis.

6. The glioblastoma multiforme group must be regarded as only slightly sensitive to irradiation. The cells show a greater resistance to irradiation than the cells of the medulloblastomas. The value of radiation treatment of these tumors is an open question. Until further information is available, we believe they should be irradiated with massive doses according to the Coutard principle, using four or five portals of entry. The time interval between treatments may be slightly longer than is advisable with the medulloblastomas.

7. Of six astrocytomas, two showed a moderate and one a mild histological response. This was seen in a more mature appearance of the cells after irradiation, an increase in multinucleated forms, and in fibrous and glial stroma.

8. Some astrocytomas are slightly radiosensitive. The results in this group warrant much more optimism concerning the rôle which irradiation may play in their treatment. They should receive thorough radiation treatment at six or eight week intervals.

9. Two ependymomas responded fairly well to treatment and showed a definite tendency to increased maturity of the cells after irradiation. Further treatment of these tumors seems indicated.

10. Three oligodendrogliomas showed no response to irradiation.

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DISCUSSION

Dr. Eugene P. Pendergrass, Philadelphia. We are particularly fortunate at the University in having a man like Dr. Alpers to work with. He has become irradiation conscious and he has done more to help us in irradiation of brain tumors than anybody else. Neurosurgeons from time to time become enthusiastic about irradiation. The patient receives one series of treatments and then goes home. As we do not have any control over them, when the patient returns he may or may not be treated. If we are to get anywhere with irradiation, there must be a close cooperation between the neurosurgeon and the radiologist.

Unfortunately, I cannot take your time to go into the irradiation factors and the treatment of these various types of gliomas. All of our patients have been inadequately treated. Some of the patients were treated for a week or ten days and then perhaps not treated again for two or three months or even for two or three years.

Dr. Alpers has been very fortunate in being able to get specimens before and after operation on 30 of these patients, and the specimens have come at a fortunate time, some of them

as early as sixteen days, some of them just a few days after irradiation was completed, and several, months or even several years later. He has made a very definite effort to evaluate the irradiation. I think it is because of this type of investigation that irradiation will be used as a real agent in attempting to control gliomas in the future. How much one will be able to do is still an unknown factor, but certainly at the present time we are giving many, many times the amount of radiation which has been used in the work that Dr. Alpers has shown you and the radiation is being given at regular intervals.

How much the skin of the head can tolerate of the type of protracted irradiation that is being given is still an unknown factor, as we haven't tried it long enough. I should like to leave with you a word of warning—that irradiation given before operation, in any similar group of patients, should only be given with the most careful and constant cooperation with the neurosurgical department, because otherwise a catastrophe may occcur from increasing the pressure which may already be increased.

Dr. W. James Gardner, Cleveland, Ohio. Neurosurgeons and roentgenologists are indebted to Dr. Cushing and Dr. Bailey for their work in differentiating various types of gliomas. The medulloblastoma is the most embryonal type of all the gliomas. The cells of this tumor most closely approximate the very youngest type of cell and, therefore, as one naturally would expect, they respond better to irradiation. The medulloblastomas occur in a very wide age range. They are most common, of course, between the ages of five and ten, but they have been found in children as young as eighteen months and in adults over forty. It has been our experience at the Cleveland Clinic that the response to irradiation does not bear any relation to the age of the patient.

Dr. Alpers has mentioned the fact that the periphery of the tumor, as far as could be determined histologically, appeared to have a greater response to irradiation than did the central portion. That, of course, is a little difficult to explain. I should like to ask him if the distant periphery of the tumor, that is, the farthest from the point of irradiation, showed as great a response as the superficial periphery of the tumor.

The question among neurological surgeons as to whether these tumors should be treated by radical removal or by biopsy and decompression is not entirely settled. There are some who feel that biopsy is all that should be done, believing that the mortality for the group and the longevity will be decidedly better if only a biopsy is done and bone removed for decompressive purposes, following which irradiation is given. However, there are those who favor the very radical excision followed by intensive irradiation.

It has been my practice to turn the patients over to the radiologist after they have recovered from operation. I feel it is only fair to the radiologist since we are asking him to treat the patient, that he should have charge of the case. In this way we can make better progress in our study of the radiosensitivity of the various types of gliomas.

Dr. Alpers (closing). Dr. Gardner brought up the question of why the periphery of the tumor was more affected than the central portion. I don't know. Dr. Chamberlin did his best to have me change my mind about that because the physics indicated that the central portion should be more affected. I think it may be due to the fact that the periphery has a better blood supply. Since the primary effect of the rays is on the blood vessels, the changes in the cells themselves are probably secondary.

I should like to enter the controversy concerning the treatment of these tumors. I cannot agree that they should be treated without some surgical manipulation. First of all, even if you do not touch these tumors they tend to spread through the subarachnoid space. My feeling would be that since irradiation does not kill the entire tumor, it would be wiser to risk spreading through the subarachnoid space, by removing as much as possible, and then treating with fractional irradiation, because massive doses do not seem to have the desired effect.

ROSTER OF DR. HENRY K. PANCOAST'S ASSOCIATES AND STUDENTS

Present Address	*Present Hospital and University Affiliations*
Eugene Abercrombie, M.D. 603 W. Main Avenue Knoxville, Tennessee Fellow: 1923–1924	
Fay Knight Alexander, M.D. Chestnut Hill Hospital Chestnut Hill, Philadelphia, Pennsylvania Fellow and Associate: April, 1930 to April, 1935.	Roentgenologist, Chestnut Hill Hospital, Philadelphia Instructor, Graduate School of Medicine, University of Pennsylvania
Kenneth D. A. Allen, M.D. 227 Sixteenth Street Denver, Colorado Fellow: 1925–1926	Private practice
Moore, Lowry Allen, M.D. Hospital of the Protestant Episcopal Church Philadelphia, Pennsylvania Fellow: September, 1931 to June, 1933	Roentgenologist, Hospital of the Protestant Episcopal Church, Philadelphia Consultant Roentgenologist, St. Christophers Hospital, Philadelphia Instructor, School of Medicine, University of Pennsylvania
John Robert Andrews, M.D. University Hospitals Cleveland, Ohio Fellow: July, 1933 to March, 1935	
Robert Phelps Barden, M.D. University Hospital 3400 Spruce Street Philadelphia, Pennsylvania Fellow: July, 1935 to the present	Instructor, School of Medicine, University of Pennsylvania
Thomas Furlong Baxter, M.D. Scituate, Massachusetts Fellow: 1922–1923	
Raymond August Berger, M.D. 1000 W. Franklin Street Richmond, Virginia Fellow: May, 1934 to November, 1935	
Harry Robert Brindle, M.D. University Hospital 3400 Spruce Street Philadelphia, Pennsylvania Fellow: November, 1936 to the present	
Herman Bryan, M.D. Temple Hill Hospital Chefoo, Shantung, China Fellow: 1921	
George Whitney Chamberlin, M.D. University Hospital 3400 Spruce Street Philadelphia, Pennsylvania Fellow: October, 1934 to October, 1936 Associate: October, 1936 to the present.	Instructor, School of Medicine, University of Pennsylvania Associate, Dept. of Radiology, University of Pennsylvania Hospital
Jacob Gershon-Cohen, M.D. 255 South 17th Street Philadelphia, Pennsylvania Fellow: July, 1926 to September, 1927	Private practice Instructor, Graduate School of Medicine, University of Pennsylvania
Carl William Cohoon, M.D. Bay Shore, New York Fellow: June, 1928 to July, 1929	
Alfred A. de Lorimier, M.D., Captain, Medical Corps, U. S. Army Gorgas Hospital Ancon, Canal Zone Fellow: 1935	
Alfred Stephen Doyle, M.D. 1726 Pine Street Philadelphia, Pennsylvania Associate: August, 1915 to March, 1923	Roentgenologist at the St. Agnes Hospital, St. Edmund's Home for Crippled Children and St. Vincent's Maternity Hospital

John Heron Edmonson, M.D. (Not in practice as roentgenologist. Internal medicine.)
929 South 20th Street
Birmingham, Alabama
Fellow: 1908

Orion Tiverton Finklea, M.D. Urologist, Florence Infirmary
200 West Evans Street
Florence, South Carolina
Fellow:

Glenn Russell Ford, M.D.
134 Washington Avenue
Endicott, New York
Fellow:

Wendell Charles Hall, M.D. Associate Roentgenologist, Temple University Hospital
Temple University Hospital Instructor, Medical School, Temple University
Philadelphia, Pennsylvania
Fellow: July, 1932 to February, 1934

Alan L. Hart, M.D. (Not practicing medicine)
901 East 43rd Street
Seattle, Washington
Fellow: 1928–1929

John H. Harris, M.D. Radiologist, Carlisle Hospital, Carlisle, Pennsylvania
414 North 2nd Street Private practice
Harrisburg, Pennsylvania
Fellow: February, 1933 to August, 1934

Percy Douglas Hay, Jr., M.D. Roentgenologist, McLeod Infirmary, Florence
115 West Cheves St.
Florence, South Carolina
Fellow: 1926–1927

Gilbert Whipple Heublein, M.D.
University Hospital
3400 Spruce Street
Philadelphia, Pennsylvania
Fellow: October, 1936 to the present

Philip Jacob Hodes, M.D. Associate, Department of Radiology, University of Pennsylvania Hospital
University Hospital Instructor, Graduate School of Medicine, University of Pennsylvania
3400 Spruce Street Instructor, School of Medicine, University of Pennsylvania
Philadelphia, Pennsylvania
Fellow: August, 1933 to August, 1936
Associate: August, 1936 to the present

John Henry Jamison, M.D.
University Hospital
3400 Spruce Street
Philadelphia, Pennsylvania
Fellow: July, 1936 to the present

Vincent C. Johnson, M.D. Assistant Professor of Roentgenology, University of Michigan Medical School
University Hospital Associate, Department of Radiology, University Hospital, Ann Arbor
Ann Arbor, Michigan
Fellow: July, 1929 to July, 1931

Karl Kornblum, M.D. Assistant Professor of Radiology, Graduate School of Medicine, University of Pennsylvania
Graduate Hospital Associate in Radiology, School of Medicine, University of Pennsylvania
Philadelphia, Pennsylvania
Associate: May, 1927 to July, 1933

Robert Henry Lowry, Jr., M.D., Major Medical Corps, U. S. Army
Sternberg General Hospital
Manila, P. I.
Fellow: April, 1927 to October, 1927

Garrett R. Miller, M.D. (Deceased)
Fellow: July, 1929 to April, 1932

John Jay Moore, M.D., Major Medical Corps, U. S. Army
Letterman General Hospital
San Francisco, California
Fellow: October, 1920 to December, 1921

George Ernest Mott, M.D., Lieutenant Commander, U. S. Navy
Naval Medical School
Washington, D. C.
Fellow:

Leslie H. Osmond, M.D. Roentgenologist, St. Francis Hospital, Pittsburgh

St. Francis Hospital
Pittsburgh, Pennsylvania
Fellow: July, 1932 to March, 1934

Eugene P. Pendergrass, M.D. — Associate, Department of Radiology, University of Pennsylvania Hospital
University Hospital — Professor of Radiology, School of Medicine, University of Pennsylvania
3400 Spruce Street — Professor of Radiology, Graduate School of Medicine, University of Pennsylvania
Philadelphia, Pennsylvania
Associate: 1919 to the present

De Alton Burr Potter, M.D. — (Deceased)
Fellow:

Ralph Rhett Rathbone, M.D. — Associate Roentgenologist, Garfield Memorial Hospital, Washington
1835 Eye Street, N.W.
Washington, D. C.
Fellow: July, 1931 to June, 1933

William B. G. Ray, M.D.
110 E. Stockton Avenue
Pittsburgh, Pennsylvania
Fellow: 1915

Edward Schons, M.D.
25 West 4th Street
St. Paul, Minnesota
Fellow: September, 1917 to December, 1917

Robert Dubs Swab, M.D.
23 E. Walnut Street
Lancaster, Pennsylvania
Fellow: 1919

James H. West, M.D.
10515 Carnegie Avenue
Cleveland, Ohio
Fellow: January, 1923 to January, 1924

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Thirty-eighth Annual Meeting: Chicago, Ill., Sept. 13–17, 1937.

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Janeway Lecture Committee: Curtis F. Burnam, Chairman, Baltimore, Md.

Representative on The American Board of Radiology: Rollin H. Stevens, Detroit, Mich.

Twenty-third Annual Meeting, 1938: To be announced.

SOCIETY PROCEEDINGS, CORRESPONDENCE AND NEWS ITEMS

Items for this section solicited promptly after the events to which they refer.

MEETINGS OF ROENTGEN SOCIETIES*

UNITED STATES OF AMERICA

AMERICAN ROENTGEN RAY SOCIETY
Secretary, Dr. E. P. Pendergrass, University Hospital, Philadelphia, Pa. Annual Meeting: Chicago, Ill., Sept. 13–17, 1937.

AMERICAN COLLEGE OF RADIOLOGY
Secretary, Dr. E. L. Jenkinson, 1439 S. Michigan Ave., Chicago, Ill. Annual meeting: Chicago, Ill., September, 1937.

SECTION ON RADIOLOGY, AMERICAN MEDICAL ASSOCIATION
Secretary, Dr. J. T. Murphy, 421 Michigan St., Toledo, Ohio. Annual meeting, 1938: To be announced.

RADIOLOGICAL SOCIETY OF NORTH AMERICA
Secretary, Dr. D. S. Childs, 607 Medical Arts Bldg., Syracuse, N. Y. Annual meeting: Chicago, Ill., Sept. 13–17, 1937.

RADIOLOGICAL SECTION, BALTIMORE CITY MEDICAL SOCIETY
Secretary, Dr. Howard H. Ashbury, Baltimore. Meets third Tuesday each month, September to May.

RADIOLOGICAL SECTION, CONNECTICUT STATE MEDICAL SOCIETY
Secretary, Dr. Max Climan, 242 Trumbull St., Hartford, Conn. Meets twice annually in May and September. Special meetings may be called by the Chairman.

RADIOLOGICAL SECTION, LOS ANGELES COUNTY MEDICAL SOCIETY
Secretary, E. N. Liljedahl, Los Angeles, Calif. Meets on the second Wednesday of each month at the County Society Building.

RADIOLOGICAL SECTION, SOUTHERN MEDICAL ASSOCIATION
Secretary, Dr. Roy G. Giles, Temple, Texas.

BROOKLYN ROENTGEN RAY SOCIETY
Secretary, Dr. E. Mendelson, 120 E. 19th St., Brooklyn, N. Y. Meets monthly on first Tuesday, October to April.

BUFFALO RADIOLOGICAL SOCIETY
Secretary-Treasurer, Dr. Joseph S. Gian-Franceschi, 610 Niagara St., Buffalo, N. Y. Meets second Monday of each month except during summer months, place of meeting selected by the host.

CHICAGO ROENTGEN SOCIETY
Secretary, Dr. R. G. Willy, 1138 N. Leavitt. Meets second Thursday of each month October to May inclusive at the Palmer House.

CINCINNATI RADIOLOGICAL SOCIETY
Secretary, Dr. H. G. Reineke, General Hospital Cincinnati, Ohio. Meets third Monday of each month, October to May, inclusive.

CLEVELAND RADIOLOGICAL SOCIETY
Secretary, Dr. North W. Shetter, 14600 Detroit Ave. Meetings are held at 6:30 P.M. at the Cleveland Chamber of Commerce Club rooms on the fourth Monday of each month from October to April, inclusive.

DENVER RADIOLOGICAL CLUB
Secretary, Dr. N. B. Newcomer, 306 Republic Bldg., Denver, Colo.
Meets on the third Tuesday of each month.

DETROIT ROENTGEN RAY AND RADIUM SOCIETY
Secretary, Dr. E. R. Witwer, Harper Hospital. Meets monthly on first Thursday from October to May, at Wayne Country Medical Society Building.

FLORIDA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. Harold O. Brown, Tampa, Florida. Meetings held twice a year, May and November.

ILLINOIS RADIOLOGICAL SOCIETY
Secretary, Dr. Cesare Gianturco, 602 W. University Ave., Urbana, Ill. Regular meetings held quarterly.

INDIANA ROENTGEN SOCIETY
Secretary, Dr. C. C. Taylor, Indianapolis, Ind. Meeting held the second Sunday in May annually.

LONG ISLAND RADIOLOGICAL SOCIETY
Secretary, Dr. S. G. Schenck, 115 Eastern Parkway, Brooklyn, N. Y. Meets at Kings County Med. Soc. Bldg. on third Thursday of each month from October to May, at 8:30 P.M.

MICHIGAN ASSOCIATION OF ROENTGENOLOGISTS
Secretary, Dr. C. S. Davenport, St. Lawrence Hospital, Lansing, Mich. Three meetings a year, Fall, Winter, and Spring.

MILWAUKEE ROENTGEN RAY SOCIETY
Secretary, Dr. S. A. Morton, Columbia Hospital, Milwaukee, Wis. Meets monthly. Place of meeting named by the president.

MINNESOTA RADIOLOGICAL SOCIETY
Secretary, Dr. H. M. Weber, Mayo Clinic, Rochester, Minn.

NEBRASKA STATE RADIOLOGICAL SOCIETY
Secretary, Dr. D. A. Dowell, Medical Arts Bldg., Omaha, Nebr. Meets third Wednesday evening of each month.

NEW ENGLAND ROENTGEN RAY SOCIETY
Secretary, Dr. E. C. Vogt, 300 Longwood Ave., Boston, Mass. Meets monthly on third Friday, Boston Medical Library.

RADIOLOGICAL SOCIETY OF NEW JERSEY
Secretary, Dr. P. S. Avery, New Brunswick, N. J. Meets annually at time and place of State Medical Society. Mid-year meetings at place designated by the president.

NEW YORK ROENTGEN SOCIETY
Secretary, Dr. R. W. Lewis, 140 E. 54th St., New York. Meets monthly on third Monday, New York Academy of Medicine, at 8:00 P.M.

NORTH CAROLINA ROENTGEN RAY SOCIETY
Secretary, Dr. Major Fleming, Rocky Mount, N. C. Annual meeting at time and place of State Medical Society. Mid-year scientific meeting at place designated.

CENTRAL NEW YORK ROENTGEN RAY SOCIETY
Secretary, Dr. C. F. Potter, 820 S. Crouse Ave., Syracuse, N. Y. Three meetings a year—January, May, and November.

PACIFIC ROENTGEN CLUB
Secretary, Dr. L. H. Garland, 450 Sutter St., San Francisco, Calif. Meets annually, during meeting of California Medical Association.

PENNSYLVANIA RADIOLOGICAL SOCIETY
Secretary, Dr. L. E. Wurster, Williamsport, Pa.

PHILADELPHIA ROENTGEN RAY SOCIETY
Secretary, Dr. B. R. Young, Temple University Hospital. Meeting first Thursday of each month from October to May inclusive, at 8:15 P.M., in Thompson Hall, College of Physicians, 19 S. 22d St.

ROCHESTER ROENTGEN RAY SOCIETY, ROCHESTER, N. Y.
Secretary, Dr. Camp C. Thomas, 476 Lake Ave. Meets on second Thursday from October to May, inclusive, 8 P.M., Rochester Academy of Medicine Building.

ST. LOUIS ROENTGEN RAY SOCIETY
Secretary, Dr. P. C. Schnoebelen, Missouri Bldg., St. Louis, Mo. Meets first week of each month. Time and place of meetings designated by president.

SOUTH CAROLINA X-RAY SOCIETY
Secretary, Dr. R. B. Taft, 105 Rutledge Ave., Charleston. Meets at time and place of South Carolina State Medical Association.

TENNESSEE RADIOLOGICAL SOCIETY
Secretary, Dr. F. B. Bogart, 311 Medical Arts Bldg.

* Secretaries of Societies not here listed are requested to send the necessary information to the Editor.

Chattanooga, Tenn. Meets annually at the time and place of the Tennessee State Medical Association.

Texas Radiological Society
Secretary, Dr. M. H. Glover, 414 Hamilton Bldg., Wichita Falls, Texas. Meets twice a year.

University of Michigan Department of Roentgenology Staff Meeting
Secretary, Dr. C. B. Peirce, University Hospital, Ann Arbor, Mich. Meets each Monday evening from September to June, at 7 P.M. at University Hospital.

University of Wisconsin Radiological Conference
Secretary, Dr. E. A. Pohle, 1300 University Ave., Madison, Wis. Meets every Thursday from 4:00–5:00 P.M., Room 301, Service Memorial Institute.

Virginia Roentgen Ray Club
Secretary, Dr. V. W. Archer, University Hospital, University, Va.
Meets annually in October.

Cuba

Sociedad Cubana de Radiologia y Fisioterapia
Secretary, Dr. Francisco Padron, Enrique, Villuendas 64, Havana, Cuba. Meets monthly in Havana.

British Empire

British Institute of Radiology Incorporated with the Röntgen Society
Meets on the third Thursday of each month, from November to June inclusive, at 8:15 P.M., at 32 Welbeck St., London, W. 1, or as advertised.

Section of Radiology of the Royal Society of Medicine (Confined to Medical Members)
Meets on the third Friday of each month during the winter at 8:15 P.M. at the Royal Society of Medicine, 1, Wimpole St., London, W. 1.

Section of Radiology and Medical Electricity, Australasian Medical Congress
Secretary, Dr. H. M. Cutler, 139 Macquarie St., Sydney, New South Wales.

Radiological Section of the Victorian Branch of the British Medical Association
Secretary, Dr. Keith Hallam, St. George's Hospital, K.E.W., Melbourne, E. 4, Victoria, Australia. Meets monthly from March to Nov. incl. for scientific discussions.

Section on Radiology, Canadian Medical Association
Secretary, Dr. A. C. Singleton, Medical Arts Bldg., Toronto 5, Ontario.

Radiological Section, New Zealand British Medical Association
Secretary, Dr. P. C. Fenwick, The Hospital, Christchurch. Meets annually.

Continental Europe

Belgian Society of Roentgenology
Secretary, Dr. J. Boine, Avenue des Alliés, 134, Louvain (Belgium).
Meets monthly on second Sunday at d'Egmonds Palace, Brussels, except in the summertime.

Sociedad Española de Radiologia y Electrologia
Secretary, Dr. J. Martin-Crespo, Fuencarral, 7, Madrid, Spain. Meets monthly in Madrid.

Société de Radiologie Médicale de France
Meets monthly on second Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Société Suisse de Radiologie (Schweizerische Röntgen-Gesellschaft)
Secretary for French language, Dr. A. Grosjean, La Chaux de Fonds.
Secretary for German language, Dr. Scheurer, Molzgasse, Biel.
Meets annually in different cities.

Société Francaise d'Electrothérapie et de Radiologie Médicale
Meets monthly on fourth Tuesday, except during months of August and September, 12 Rue de Seine, Paris.

Association of German Roentgenologists and Radiologists in Czecho-Slovakia
Secretary, Dr. Walter Altschul, German University, Prague, 11.52.

Deutsche Röntgen-Gesellschaft (Gesellschaft für Röntgenkunde und Strahlenforschung)
Meets annually in April, alternating one year in Berlin, one year in some other German city. Meets in addition every two years with the Gesellschaft deutscher Naturforscher und Aerzte.
Permanent secretary, Professor Dr. Haenisch, Klopstockstrasse 10, Hamburg, Germany.

Süd- und Westdeutsche Röntgengesellschaft
Meets annually in different cities.

Nord- und Ostdeutsche Röntgengesellschaft
Meets annually in different cities.

Dutch Society of Electrology and Roentgenology
Holds two meetings a year in Amsterdam, one in the Spring, and one in the Fall.

Societa Italiana Radiologia Medica
Secretary, Professor M. Ponzio, University of Turin, Turin.

Societatea Romana de Radiologie si Electrologie
Secretary, Dr. Oscar Meller, Str. Banul Mărăcine, 30, S. I., Bucuresti, Roumania.
Meets second Monday in every month with the exception of July and August.

All-Russian Roentgen Ray Association, Leningrad, USSR in the State Institute of Roentgenology and Radiology, 6 Roentgen St.
Secretaries, Drs. S. A. Reinberg and S. G. Simonson, Meets annually.

Leningrad Roentgen Ray Society
Secretaries, Drs. S. G. Simonson and G. A. Gusterin.
Meets monthly, first Monday at 8 o'clock State Institute of Roentgenology and Radiology, Leningrad.

Moscow Roentgen Ray Society
Secretaries, Drs. L. L. Holst, A. W. Ssamygin and S. T. Konobejevsky.
Meets monthly on the first Monday at 8 o'clock, the place of meeting being selected by the Society.

Polish Society of Radiology
Secretary, Dr. Jan. Kochanowski, 45 Gornoslazka St., Warsaw. Meets annually.

Warsaw Section, Polish Society of Radiology
Secretary, Dr. B. Krynski, 11 Zielna St.
Meets once a month except in the summertime.

Scandinavian Roentgen Societies
The Scandinavian roentgen societies have formed a joint association called the Northern Association for Medical Radiology, meeting every second year in the different countries belonging to the Association. Each of the following societies, with exception of the Denmark Society, meets every second month except in the summertime.

Society of Medical Radiology in Sweden
Meets in Stockholm.

Society of Medical Radiology in Norway
Meets in Oslo.

Society of Medical Radiology in Denmark
Secretary, Dr. G. Biering, Copenhagen.
Meets on the second Wednesday of each month from October to July in Copenhagen, at 8 o'clock in the State Institute of Roentgenology.

Society of Medical Radiology in Finland
Meets in Helsingfors.

Vienna Roentgen Society
Meets first Wednesday of each month, at 6.30 P.M. at Zentral-Röntgen Institut des allgemeinen Krankenhauses Alserstrasse 4.

Orient

Japan X-Ray Association
c/o Orthopedic Surgery, Tokyo Imperial University.
Meets annually in April.

Kinki Roentgen-Abend Society
Director, Dr. Prof. Taiga Saito, Ogawaoike Tyoto Japan. Meets bi-monthly on third Sunday.